0 L 57 L 5 AAAO/DTO				Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	1	of	47	Attorney Docket Number	ISIS-5027	

	U. S. PATENT DOCUMENTS								
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear				
	1	2002/0049173 A1	04-25-2002	Bennett et al.					
	2	2002/0068708 A1	06-06-2002	Wengel et al.					
	3	2002/0071826 A1	06-13-2002	Tamarkin et al.					
	4	2002/0081577 A1	06-27-2002	Kilkuskie et al.					
	5	2002/0081736 A1	06-27-2002	Conroy et al.					
	6	2002/0102267 A1	08-01-2002	Lu et al.					
	7	2002/0132788 A1	09-19-2002	Lewis et al.					
	8	2002/0147332 A1	10-10-2002	Kaneko					
	9	2002/0156235 A1	10-24-2002	Manoharan et al.					
	10	2002/0160393 A1	10-31-2002	Symonds et al.					
	11	2002/0162126 A1	10-30-2002	Beach et al.					
	12	2002/0165189 A1	11-07-2002	Crooke					
	13	2002/1051512 A1	10-17-2002	Peyman et al.					
	14	2003/0004325 A1	01-02-2003	Cook et al.					
	15	2003/0027780 A1	02-06-2003	Hardee et al.					
	16	2003/0096286 A1	05-22-2003	Crooke					
	17	2003/0096287 A1	05-22-2003	Crooke					
	18	2003/0096784 A1	05-22-2003	Crooke					
	19	2003/0119777 A1	06-26-2003	Crooke					
	20	2003/0158403 A1	08-21-2003	Manoharan et al.					
	21	2003/0166282 A1	09-04-2003	Brown et al.					
	22	2003/0175906 A1	09-18-2003	Manoharan et al.					
	23	2003/0187240 A1	10-02-2003	Cook et al.					
	24	2003/0190635 A1	10-09-2003	McSwiggen					

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	2	of	47	Attorney Docket Number	ISIS-5027	

	U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			
	25	2003/0207804 A1	11-06-2003	Manoharan et al.				
	26	2003/0224377 A1	12-04-2003	Wengel et al.				
	27	2004/0001811 A1	01-01-2004	Kreutzer et al.				
	28	2004/0009938 A1	01-15-2004	Manoharan et al.				
	29	2004/0014957 A1	01-22-2004	Eldrup et al.				
	30	2004/0018999 A1	01-29-2004	Beach et al.				
	31	2004/0102618 A1	05-27-2004	Crooke et al.				
	32	2004/0171033 A1	09-02-2004	Baker et al.				
	33	2004/0259247 A1	12-23-2004	Tuschl et al.				
	34	2005/0020525 A1	01-27-2005	McSwiggen et al.				
	35	2005/0080246 A1	04-14-2005	Allerson et al.				
	36	2005/0164209 A1	07-28-2005	Bennett et al.				
	37	2005/0181382 A1	08-18-2005	Zamore et al.				
	38	2005/0221275 A1	10-06-2005	Bennett et al.				
	39	2005/0245474 A1	11-03-2005	Baker et al.				
	40	2005/0273868 A1	12-08-2005	Rana				
	41	2006/0127891 A1	06-15-2006	McSwiggen et al.				
	42	2007/0032446 A1	02-08-2007	Cook et al.				
	43	4,381,344	04-26-1983	Rideout et al.				
	44	4,415,732	11-15-1983	Caruthers et al.				
	45	4,426,330	01-17-1984	Sears				
	46	4,458,066	07-03-1984	Caruthers et al.				
	47	4,476,301	10-09-1954	Imbach et al.				
	48	4,500,707	02-19-1985	Caruthers et al.				

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	3	of	47	Attorney Docket Number	ISIS-5027	

U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No. Document Number  Number – Kind Code (if known)		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	49	4,511,713	04-16-1985	Miller et al.			
	50	4,534,899	08-13-1985	Sears			
	51	4,587,044	05-06-1986	Miller			
	52	4,605,735	08-12-1986	Miyoshi			
	53	4,667,025	05-19-1987	Miyoshi			
	54	4,668,777	05-26-1987	Caruthers et al.			
	55	4,689,320	08-25-1987	Kaji			
	56	4,725,677	02-16-1988	Koster et al.			
	57	4,760,017	07-26-1988	McCormick			
	58	4,762,779	08-09-1988	Snitman			
	59	4,789,737	12-06-1988	Miyoshi			
	60	4,824,941	04-25-1989	Gordon			
	61	4,828,979	05-09-1989	Klevan			
	62	4,835,263	05-30-1989	Nguyen			
	63	4,845,205	07-04-1989	Huynh Dinh et al.			
	64	4,849,320	07-18-1989	Irving et al.			
	65	4,849,513	07-18-1989	Smith et al.			
	66	4,876,335	10-24-1989	Yamane			
	67	4,904,582	02-27-1990	Tullis			
	68	4,924,624	05-15-1990	Suhadolnik et al.			
	69	4,948,882	08-14-1990	Ruth			
	70	4,958,013	09-18-1990	Letsinger			
	71	4,965,350	10-23-1990	Inoue et al.			
	72	4,973,679	11-27-1990	Caruthers et al.			

Examiner	Date	
Signature	Considered	

	1.4.0/DTO			Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT  (use as many sheets as necessary)				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
				Examiner Name	Sean McGarry	
Sheet	4	of	47	Attorney Docket Number	ISIS-5027	

	U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			
	73	4,981,957	01-01-1991	Lebleu				
	74	5,000,000	03-19-1991	Ingram et al.				
	75	5,013,556	05-07-1991	Woodle et al.				
	76	5,034,506	07-23-1991	Summerton et al.				
	77	5,082,830	01-21-1992	Brakel				
	78	5,108,921	04-28-1992	Low et al.				
	79	5,109,124	04-28-1992	Ramathandran				
	80	5,112,963	05-12-1992	Pieles				
	81	5,118,800	06-02-1992	Fung				
	82	5,118,802	06-02-1992	Smith				
	83	5,132,418	07-21-1992	Caruthers et al.				
	84	5,134,066	07-28-1992	Rogers et al.				
	85	5,138,045	08-11-1992	Cook				
	86	5,149,782 A	09-22-1992	Chang et al.				
	87	5,166,315	11-24-1992	Summerton et al.				
	88	5,175,273	12-29-1992	Bischofberger et al.				
	89	5,177,196	01-05-1993	Meyer, Jr. et al.				
	90	5,185,444	02-09-1993	Summerton et al.				
	91	5,188,897	02-23-1993	Suhadolnik et al.				
	92	5,194,599	03-16-1993	Froehler et al.				
	93	5,212,295 A	05-18-1993	Cook				
	94	5,213,804	05-25-1993	Martin et al.				
	95	5,214,134	05-25-1993	Weis et al.				
	96	5,214,135 A	05-25-1993	Srivastava et al.				

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
	<del>_</del>	DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT  (use as many sheets as necessary)				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
				Examiner Name	Sean McGarry	
Sheet	5	of	47	Attorney Docket Number	ISIS-5027	

U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	97	5,214,136	05-25-1993	Lin			
	98	5,216,141	06-01-1993	Benner			
	99	5,218,105	06-08-1993	Cook			
	100	5,220,007	06-15-1993	Pederson			
	101	5,227,170	07-13-1993	Sullivan			
	102	5,245,022	09-14-1993	Weis			
	103	5,254,469	10-19-1993	Warren			
	104	5,258,506	11-02-1993	Urdea			
	105	5,262,536	11-16-1993	Hobbs			
	106	5,264,221	11-23-1993	Tagawa et al.			
	107	5,264,423	11-23-1993	Cohen et al			
	108	5,272,250	12-21-1993	Spielvogel			
	109	5,276,019	01-04-1994	Cohen et al			
	110	5,278,302	01-11-1994	Caruthers et al.			
	111	5,286,717	02-15-1994	Cohen et al			
	112	5,292,873	03-08-1994	Rokita			
	113	5,317,098	05-31-1994	Shizuya			
	114	5,319,080	06-07-1994	Leumann			
	115	5,321,131	06-14-1994	Agrawal et al.			
	116	5,354,844	10-11-1994	Beug et al.			
	117	5,356,633	10-18-1994	Woodle et al.			
	118	5,367,066	11-22-1994	Urdea et al.			
	119	5,371,241	12-06-1994	Brush			
	120	5,391,723	02-21-1995	Priest			

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT  (use as many sheets as necessary)				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
				Examiner Name	Sean McGarry	
Sheet	6	of	47	Attorney Docket Number	ISIS-5027	

U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	121	5,393,878	02-28-1995	Leumann			
	122	5,395,619	03-07-1995	Zalipsky et al.			
	123	5,399,676	03-21-1995	Froehler et al.			
	124	5,405,938	04-11-1995	Summerton et al.			
	125	5,405,939	04-11-1995	Suhadolnik et al.			
	126	5,414,077	05-09-1995	Lin			
	127	5,416,016	05-16-1995	Low et al.			
	128	5,416,203	05-16-1995	Letsinger			
	129	5,417,978	05-23-1995	Tari et al.			
	130	5,432,272	07-11-1995	Benner			
	131	5,434,257	07-18-1995	Matteucci et al.			
	132	5,446,137	08-29-1995	Maag			
	133	5,451,463	09-19-1995	Nelson			
	134	5,453,496	09-26-1995	Caruthers et al.			
	135	5,455,233	10-03-1995	Spielvogel et al.			
	136	5,457,187	10-10-1995	Gmeiner et al.			
	137	5,459,127	10-17-1995	Felgner et al.			
	138	5,462,854	10-31-1995	Coassin et al.			
	139	5,466,677	11-14-1995	Baxter et al.			
	140	5,469,854	11-28-1995	Unger et al.			
	141	5,470,967	11-28-1995	Huie et al.			
	142	5,486,603	01-23-1996	Bahr			
	143	5,491,133	02-13-1996	Walder			
	144	5,502,177	03-26-1996	Matteucci et al.			

Examiner	Date	
Signature	Considered	

	1440/PTO	_		Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	7	of	47	Attorney Docket Number	ISIS-5027	

	U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			
	145	5,510,475	04-23-1996	Agrawal				
	146	5,512,295	04-30-1996	Kornberg et al.				
	147	5,512,439	04-30-1996	Hornes				
	148	5,512,667	04-30-1996	Reed				
	149	5,514,785	05-07-1996	Van Ness				
	150	5,519,126	05-21-1996	Hecht				
	151	5,521,291	05-28-1996	Curiel et al.				
	152	5,525,465	06-11-1996	Haralambidis				
	153	5,525,711	06-11-1996	Hawkins et al.				
	154	5,527,528	06-18-1996	Allen et al.				
	155	5,527,899	06-18-1996	Froehler				
	156	5,532,130	07-02-1996	Alul				
	157	5,534,259	07-09-1996	Zalipsky et al.				
	158	5,536,821	07-16-1996	Agrawal et al.				
	159	5,539,082	07-23-1996	Nielsen et al.				
	160	5,541,306	07-30-1996	Agrawal et al.				
	161	5,541,307	07-30-1996	Cook et al.				
	162	5,541,313	07-30-1996	Ruth				
	163	5,543,152	08-06-1996	Webb et al.				
	164	5,543,158	08-06-1996	Gref et al.				
	165	5,545,730	08-13-1996	Urdea				
	166	5,547,932	08-20-1996	Curiel et al.				
	167	5,550,111	08-27-1996	Suhadolnik et al.				
	168	5,552,538	09-13-1996	Urdea				

Examiner	Date	
Signature	Considered	

	1.4.0/DTO			Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT  (use as many sheets as necessary)				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
				Examiner Name	Sean McGarry	
Sheet	8	of	47	Attorney Docket Number	ISIS-5027	

	U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			
	169	5,552,540	09-03-1996	Haralambidis				
	170	5,556,948	09-17-1996	Tagawa et al.				
	171	5,561,225	10-01-1996	Maddry et al.				
	172	5,563,253	10-08-1996	Agrawal et al.				
	173	5,565,350	10-15-1996	Kmiec				
	174	5,565,552	10-15-1996	Magda				
	175	5,565,555	10-15-1996	Froehler et al.				
	176	5,567,810	10-22-1996	Weis				
	177	5,567,811	10-22-1996	Misiura et al.				
	178	5,571,799	11-05-1996	Tkachuk et al.				
	179	5,574,142	11-12-1996	Meyer				
	180	5,576,302 A	11-19-1996	Cook et al.				
	181	5,576,427	11-19-1996	Cook et al.				
	182	5,578,717	11-26-1996	Urdea				
	183	5,578,718	11-26-1996	Cook				
	184	5,580,575	12-03-1996	Unger et al.				
	185	5,580,731	12-03-1996	Chang				
	186	5,582,188 A	12-10-1996	Benderev et al.				
	187	5,583,020	12-17-1996	Arnold, Jr. et al.				
	188	5,585,481	12-17-1996	Arnold				
	189	5,587,361	12-24-1996	Cook et al.				
	190	5,587,371	12-24-1996	Sessler				
	191	5,587,469	12-24-1996	Cook et al.				
	192	5,591,584	01-07-1997	Chang				

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
		I DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT  (use as many sheets as necessary)				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
				Examiner Name	Sean McGarry	
Sheet	9	of	47	Attorney Docket Number	ISIS-5027	

	U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			
	193	5,591,721	01-07-1997	Agrawal et al.				
	194	5,591,722	01-07-1997	Montgomery et al.				
	195	5,594,121	01-14-1997	Froehler et al.				
	196	5,595,726	01-21-1997	Magda				
	197	5,595,756	01-21-1997	Bally et al.				
	198	5,596,086	01-21-1997	Matteucci et al.				
	199	5,596,091	01-21-1997	Switzer et al.				
	200	5,597,696	01-28-1997	Linn				
	201	5,597,909	01-28-1997	Urdea				
	202	5,599,797 A	02-04-1997	Cook et al.				
	203	5,599,923	02-04-1997	Sessler				
	204	5,599,925	02-04-1997	Torii				
	205	5,599,928	02-04-1997	Hemmi et al.				
	206	5,602,240	02-11-1997	De Mesmaeker et al.				
	207	5,607,922	03-04-1997	De Clercq et al.				
	208	5,607,923 A	03-04-1997	Cook et al.				
	209	5,608,046	03-04-1997	Cook				
	210	5,610,289	03-11-1997	Cook et al.				
	211	5,610,300	03-11-1997	Altmann				
	212	5,612,469 A	03-18-1997	Goodchild				
	213	5,614,621	03-25-1997	Ravikumar et al.				
	214	5,618,704	04-08-1997	Sanghvi et al.				
	215	5,623,065 A	04-22-1997	Cook et al.				
	216	5,623,070	04-22-1997	Cook et al.				

Examiner	Date	
Signature	Considered	

	1.4.0/DTO			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT  (use as many sheets as necessary)				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
				Examiner Name	Sean McGarry	
Sheet	10	of	47	Attorney Docket Number	ISIS-5027	

	U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			
	217	5,625,050	04-29-1997	Beaton et al.				
	218	5,627,053	05-06-1997	Usman				
	219	5,633,360	05-27-1997	Bischofberger et al.				
	220	5,634,488 A	06-03-1997	Martin, Jr.				
	221	5,635,488 A	06-03-1997	Cook et al.				
	222	5,639,647 A	06-17-1997	Usman et al.				
	223	5,643,889 A	07-01-1997	Suhadolnik et al.				
	224	5,645,985	07-08-1997	Froehler et al.				
	225	5,646,265	07-08-1997	Mcgee				
	226	5,646,269	07-08-1997	Matteucci et al.				
	227	5,652,355	07-29-1997	Metelev				
	228	5,652,356	07-29-1977	Agrawal				
	229	5,658,731 A	08-19-1997	Sproat et al.				
	230	5,658,873	08-19-1997	Bertsch-Frank				
	231	5,661,134 A	08-26-1997	Cook et al.				
	232	5,663,312	09-02-1997	Chaturvedula				
	233	5,663,360 A	09-02-1997	Bortolaso et al.				
	234	5,670,633	09-23-1977	Cook et al.				
	235	5,672,662 A	09-30-1997	7 Harris et al.				
	236	5,672,695 A	09-30-1997	7 Eckstein et al.				
	237	5,672,697	09-30-1997	Buhr et al.				
	238	5,677,289 A	10-14-1997	Torrence et al.				
	239	5,677,437	10-14-1997	Teng et al.				
	240	5,677,439	10-14-1997	Weis et al.				

Examiner	Date	
Signature	Considered	

	1.10/DT0			Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	11	of	47	Attorney Docket Number	ISIS-5027	

U. S. PATENT DOCUMENTS								
Examiner Initials	Cite No. Document Number  Number – Kind Code (if known)		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			
	241	5,681,940	10-28-1997	Wang et al.				
	242	5,681,941	10-28-1997	Cook et al.				
	243	5,684,142 A	11-04-1997	Mishra et al.				
	244	5,684,143 A	11-04-1997	Gryaznov et al.				
	245	5,684,243 A	11-04-1997	Gururaja et al.				
	246	5,688,941	11-18-1997	Cook				
	247	5,698,687 A	12-16-1997	Eckstein et al.				
	248	5,700,785 A	12-23-1997	Suhadolnik et al.				
	249	5,700,920	12-23-1997	Altmann				
	250	5,700,922	12-23-1997	Cook				
	251	5,714,166 A	02-03-1998	Tomalia et al.				
	252	5,714,331	02-03-1998	Buchardt et al.				
	253	5,716,824 A	02-10-1998	Beigelman et al.				
	254	5,719,262	02-17-1998	Buchardt et al.				
	255	5,721,218	02-24-1998	Froehler et al.				
	256	5,726,297 A	03-10-1998	Gryaznov et al.				
	257	5,750,666 A	05-12-1998	Caruthers et al.				
	258	5,750,669 A	05-12-1998	Rosch et al.				
	259	5,750,692	05-12-1998	Cook et al.				
	260	5,760,209	06-02-1998	Cheruvallath et al.				
	261	5,763,588	06-09-1998	Matteucci et al.				
	262	5,770,713	06-23-1998	Imbach et al.				
	263	5,770,716 A	06-23-1998	Khan et al.				
	264	5,777,092 A	07-07-1998	Cook et al.				

Examiner	Date	
Signature	Considered	

	4.40/DT0			Complete if Known		
Substitute for 1	449/PTO			Application Number	10/078,949	
	<del>_</del>	DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT  (use as many sheets as necessary)				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
				Examiner Name	Sean McGarry	
Sheet	12	of	47	Attorney Docket Number	ISIS-5027	

	U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No. Document Number  Number – Kind Code (if known)		Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			
	265	5,780,607	07-14-1998	Goodnow, Jr. et al.				
	266	5,789,576 A	08-04-1998	Daily et al.				
	267	5,792,608	08-11-1998	Swaminathan et al.				
	268	5,792,747	08-11-1998	Schally				
	269	5,792,844 A	08-11-1998	Sanghvi et al.				
	270	5,792,847 A	08-11-1998	Buhr et al.				
	271	5,801,154 A	09-01-1998	Baracchini et al.				
	272	5,808,023 A	09-15-1998	Sanghvi et al.				
	273	5,808,036 A	09-15-1998	Kool				
	274	5,817,781 A	10-06-1998	Swaminathan et al.				
	275	5,830,635 A	11-03-1998	Agnello				
	276	5,830,653	11-03-1998	Froehler et al.				
	277	5,837,835 A	11-17-1998	Gryaznov et al.				
	278	5,837,852 A	11-17-1998	Chung et al.				
	279	5,840,876 A	11-24-1998	Beigelman et al.				
	280	5,854,410	12-29-1998	Arnold Jr. et al.				
	281	5,859,221 A	01-12-1999	Cook et al.				
	282	5,872,232 A	02-16-1999	Cook et al.				
	283	5,874,553	02-23-1999	Peyman et al.				
	284	5,914,396 A	06-22-1999	Cook et al.				
	285	5,936,080 A	08-10-1999	Stec et al.				
	286	5,945,521 A	08-31-1999	Just et al.				
	287	5,965,720 A	10-12-1999	Gryaznov et al.				
	288	5,965,721 A	10-12-1999	Cook et al.				

Examiner	Date	
Signature	Considered	

	1440/PT0			Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	13	of	47	Attorney Docket Number	ISIS-5027	

U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	289	5,969,116 A	10-19-1999	Martin			
	290	5,969,118 A	10-19-1999	Sanghvi et al.			
	291	5,986,083 A	11-16-1999	Dwyer et al.			
	292	5,998,588 A	12-07-1999	Hoffman et al.			
	293	6,001,841	12-14-1999	Cook et al.			
	294	6,005,087	12-21-1999	Cook et al.			
	295	6,005,094 A	12-21-1999	Simon et al.			
	296	6,005,096	12-21-1999	Matteucci et al.			
	297	6,007,992	12-28-1999	Lin et al.			
	298	6,013,785 A	01-11-2000	Bruice et al.			
	299	6,015,886 A	01-18-2000	Dale et al.			
	300	6,020,475	02-01-2000	Capaldi et al.			
	301	6,025,140	02-15-2000	Langel et al.			
	302	6,028,183	02-22-2000	Lin et al.			
	303	6,028,188 A	02-22-2000	Arnold, Jr. et al.			
	304	6,043,060	03-28-2000	Imanishi			
	305	6,043,352 A	03-28-2000	Manoharan et al.			
	306	6,046,306	04-04-2000	Breipohl et al.			
	307	6,051,699	04-18-2000	Ravikumar			
	308	6,087,484 A	07-11-2000	Goodchild			
	309	6,096,875 A	08-01-2000	Khan et al.			
	310	6,111,085 A	08-29-2000	Cook et al.			
	311	6,117,657 A	09-12-2000	Usman et al.			
	312	6,121,437	09-19-2000	Guzaev et al.			

Examiner	Date	
Signature	Considered	

	1440/DTO	_		Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT  (use as many sheets as necessary)				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
				Examiner Name	Sean McGarry	
Sheet	14	of	47	Attorney Docket Number	ISIS-5027	

U. S. PATENT DOCUMENTS							
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	313	6,127,346	10-03-2000	Peyman et al.			
	314	6,127,533 A	10-03-2000	Cook et al.			
	315	6,147,200	11-14-2000	Manoharan et al.			
	316	6,150,510	11-21-2000	Seela et al.			
	317	6,153,737 A	11-28-2000	Manoharan et al.			
	318	6,166,188 A	12-26-2000	Cook et al.			
	319	6,169,177	01-02-2001	Manoharan			
	320	6,172,208 B1	01-09-2001	Cook			
	321	6,172,209	01-09-2001	Manoharan et al.			
	322	6,172,216 B1	01-09-2001	Bennett et al.			
	323	6,207,646	03-27-2001	Krieg et al.			
	324	6,220,025 B1	04-24-2001	Mauti et al.			
	325	6,227,982 B1	05-08-2001	Wurster			
	326	6,239,265 B1	05-29-2001	Cook			
	327	6,239,272 B1	05-29-2001	Beigelman et al.			
	328	6,262,241 B1	07-17-2001	Cook et al.			
	329	6,268,490	07-31-2001	Imanishi et al.			
	330	6,271,358 B1	08-07-2001	Manoharan et al.			
	331	6,277,634	08-21-2001	McCall et al.			
	332	6,277,967 B1	08-21-2001	Manoharan			
	333	6,281,201 B1	08-28-2001	Suhadolnik et al.			
	334	6,284,538 B1	09-04-2001	Monia et al.			
	335	6,287,860	09-11-2001	Monia et al.			
	336	6,294,522 B1	09-25-2001	Zablocki et al.			

Examiner	Date	
Signature	Considered	

	4.40/DT0			Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
	<del>_</del>	DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	15	of	47	Attorney Docket Number	ISIS-5027	

U. S. PATENT DOCUMENTS								
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear			
	337	6,300,319 B1	10-09-2001	Manoharan				
	338	6,307,040 B1	10-23-2001	Cook et al.				
	339	6,326,358 B1	12-04-2001	Manoharan				
	340	6,326,478	12-04-2001	Cheruvallath et al.				
	341	6,329,346 B1	12-11-2001	Muhlegger et al.				
	342	6,331,617 B1	12-18-2001	Weeks et al.				
	343	6,335,432 B1	01-01-2002	Segev				
	344	6,335,434 B1	01-01-2002	Guzaev et al.				
	345	6,335,437 B1	01-01-2002	Manoharan et al.				
	346	6,344,436 B1	02-05-2002	Smith et al.				
	347	6,358,931 B1	03-19-2002	Cook et al.				
	348	6,365,379 B1	04-02-2002	Lima et al.				
	349	6,380,169 B1	04-20-2002	Adams et al.				
	350	6,395,437 B1	05-28-2002	Wollesen				
	351	6,395,474 B1	05-28-2002	Buchardt et al.				
	352	6,395,492 B1	05-28-2002	Manoharan et al.				
	353	6,410,702 B1	06-25-2002	Swaminathan et al.				
	354	6,414,127	07-02-2002	Lin et al.				
	355	6,420,549 B1	07-16-2002	Cook et al.				
	356	6,426,220	07-30-2002	Bennett et al.				
	357	6,436,640 B1	08-20-2002	Simmons et al.				
	358	6,440,943 B1	08-27-2002	Cook et al.				
	359	6,444,806 B1	09-03-2002	Veerapanani et al.				
	360	6,465,628	10-15-2002	Ravikumar et al.				

Examiner	Date	
Signature	Considered	

	1.4.40/DTO			Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many sheets as necessary)			Examiner Name	Sean McGarry	
Sheet	16	of	47	Attorney Docket Number	ISIS-5027	

	U. S. PATENT DOCUMENTS						
Examiner Initials	Cite No.	Document Number Number – Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Page, Columns, Lines, Where Relevant Passages or Relevant Figures Appear		
	361	6,476,205 B1	11-05-2002	Buhr et al.			
	362	6,486,308 B2	11-26-2002	Kutyavin et al.			
	363	6,525,031 B2	02-25-2003	Manoharan			
	364	6,528,631 B1	03-04-2003	Cook et al.			
	365	6,531,584 B1	03-11-2003	Cook et al.			
	366	6,534,639 B1	03-18-2003	Manoharan et al.			
	367	6,559,279 B1	05-06-2003	Manoharan et al.			
	368	6,593,466	07-15-2003	Manoharan et al.			
	369	6,656,730	12-02-2003	Manoharan			
	370	6,670,461	12-30-2003	Wengel et al.			
	371	6,673,611 B2	01-06-2004	Thompson et al.			
	372	6,683,167 B2	01-27-2004	Metelev et al.			
	373	6,794,499	09-21-2004	Wengel et al.			
	374	6,887,906	05-03-2005	Teng et al.			
	375	RE34,069	09-15-1992	Koster et al.			

Examiner	Date	
Signature	Considered	

	Substitute for 1449/PTO			Complete if Known		
Substitute for				Application Number	10/078,949	
INFORMATION DISCLOSURE				Filing Date	02-20-2002	
STAT	STATEMENT BY APPLICANT			First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	17	of	47	Attorney Docket Number	ISIS-5027	

		FOREI	GN PATENT D	OCUMENTS		
Examiner Initials	Cite No	Foreign Patent Document Country Code- Number -Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Т
	376	CA 2,017,369 C	01-23-2001	Roche Diagnostics GmbH		
	377	DE 3915432 A1	11-15-1990	Klockner-Humboldt-Deutz AG		x
	378	DE 4110085 A1	01-10-1992	Boehringer Ingelheim Int'l. GmbH		X
	379	EP 0260032 A2	03-16-1988	Ajinmoto Co., Inc.		
	380	EP 0269574 A2	06-01-1988	Nippon Zoki Pharmaceutical Co. Ltd.		
	381	EP 0287313 A2	10-19-1988	Marquez		
	382	EP 0339330 A2	11-02-1989	Spradau, Hans F.W.		
	383	EP 0417999 A1	03-20-1991	The Wellcome Foundation Limited		
	384	EP 1389637 A1	02-18-2004	Atugen AG		
	385	WO 00/08044 A1	02-17-2000	Isis Pharmaceuticals, Inc.		
	386	WO 00/44895	08-03-2000	Kreutzer et al.		
	387	WO 00/44914	08-03-2000	Med. Coll. Of Georgia		
	388	WO 00/49035	08-24-2000	General Hospital		
	389	WO 00/76554 A1	12-21-2000	Isis Pharmaceuticals, Inc.		
	390	WO 01/049687 A2	07-12-2001	K.U. Leuven Research & Development		
	391	WO 01/29058 A1	04-26-2001	Univ Massachussetts		
	392	WO 01/36641	05-25-2001	Chiron Corp.		
	393	WO 01/36646	05-25-2001	Cancer Res. Campaign Tech.		
	394	WO 01/48183 A2	07-05-2001	Devgen NV		
	395	WO 01/75164	10-11-2001	Whitehead Inst.		
	396	WO 02/36743 A2	05-10-2002	Isis Pharmaceuticals, Inc.		

Examiner Signature Date Considered

Complete if Known Substitute for 1449/PTO **Application Number** 10/078,949 **INFORMATION DISCLOSURE** Filing Date 02-20-2002 **STATEMENT BY APPLICANT First Named Inventor** Stanley T. Crooke **Art Unit** 1635 Sean McGarry **Examiner Name** (use as many sheets as necessary) Sheet 18 47 **Attorney Docket Number** ISIS-5027 of

		FOREI	GN PATENT D	OCUMENTS		
Examiner Initials	Cite No	Foreign Patent Document Country Code- Number -Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Т
	397	WO 02/38578 A1	05-16-2002	Chattopadhyaya		
	398	WO 03/004602 A2	01-16-2003	Isis Pharmaceuticals, Inc.		
	399	WO 03/070918 A2	08-28-2003	Ribozyme Pharm Inc.		
	400	WO 03/072705 A2	09-04-2003	Sirna Therapeutics, Inc.		
	401	WO 2004/015107 A2	02-19-2004	Atugen AG		
	402	WO 2004/041889 A2	05-21-2004	Isis Pharm.		
	403	WO 2004/043977 A2	05-27-2004	Isis Pharm.		
	404	WO 2004/043978 A2	05-27-2004	Isis Pharm.		
	405	WO 2004/043979 A2	05-27-2004	Isis Pharm.		
	406	WO 2004/044133 A2	05-27-2004	Isis Pharm.		
	407	WO 2004/044136 A2	05-27-2004	Isis Pharm.		
	408	WO 2004/044138 A2	05-27-2004	Isis Pharm.		
	409	WO 2004/044139 A2	05-27-2004	Isis Pharmaceuticals Inc.		
	410	WO 2004/044140 A2	05-27-2004	Isis Pharm.		
	411	WO 2004/083430 A2	09-30-2004	Elmen et al.		
	412	WO 2004/097049 A1	11-11-2004	Isis Pharmaceuticals, Inc.		
	413	WO 2004/113496 A2	12-29-2004	Isis Pharm.		
	414	WO 2005/027962 A2	03-31-2005	Isis Pharm.		
	415	WO 86/05518 A1	09-25-1986	Summerton et al.		
	416	WO 89/12060 A1	12-14-1989	Benner		
	417	WO 90/15814 A1	12-27-1990	Meiogenics, Inc.		
	418	WO 91/06556 A1	05-16-1991	Gilead Sciences, Inc.		
	419	WO 91/10671 A1	07-25-1991	Isis Pharmaceuticals, Inc.		

Examiner	Date	
Signature	Considered	

	1.4.4.0./DT-0	_		Complete if Known		
Substitute for 1	Substitute for 1449/PTO			Application Number	10/078,949	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Filing Date	02-20-2002	
			ANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	19	of	47	Attorney Docket Number	ISIS-5027	

		FORE	IGN PATENT [	OCUMENTS		
Examiner Initials	Cite No	Foreign Patent Document Country Code- Number -Kind Code (if known)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	Т
	420	WO 91/15499 A1	10-17-1991	Europaisches Laboratorium Fur Molekularbiologie		
	421	WO 92/02258 A1	02-20-1992	Isis Pharmaceuticals, Inc.		
	422	WO 92/03452 A1	03-05-1992	Isis Pharmaceuticals, Inc.		
	423	WO 92/03568 A1	03-05-1992	Isis Pharmaceuticals, Inc.		
	424	WO 93/24510 A1	12-09-1993	Centre National de la Recherche		
	425	WO 94/23026 A1	10-13-1994	Genset SA		
	426	WO 94/26764 A1	11-24-1994	Centre National de la Recherche		
	427	WO 96/11205	04-18-1996	Isis Pharmaceuticals, Inc.		
	428	WO 97/26270 A2	07-24-1997	Ribozyme Pharm.		
	429	WO 97/30064 A1	08-21-1997	Stichting REGA		
	430	WO 98/16550 A1	04-23-1998	Isis Innovation Limited		
	431	WO 98/39352 A1	09-11-1998	Imanishi		
	432	WO 98/52614 A2	11-26-1998	The Board of Trustees of the Leland Stanford Junior Univ.		
	433	WO 99/14226 A2	03-25-1999	Exiqon A S		
	434	WO 99/32619 A1	07-01-1999	Carnegie Institute		

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
	RMATION			Filing Date	02-20-2002	
STA	STATEMENT BY APPLICANT			First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many sheets as necessary)			Examiner Name	Sean McGarry	
Sheet	20	of	47	Attorney Docket Number	ISIS-5027	

		NON PATENT LITERATURE DOCUMENTS					
Examiner Initials	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), Volume-issue Number(s), publisher, city and/or country where published.					
	435	Abe, A., et al., "Conformational energies and the random-coil dimensions and dipole moments of the polyoxides CH3O[CH2)yO]xCH3," J. Am. Chem. Soc., 1976, 98(21), 6468-6476					
	436	Afonina, I. et al., "Sequence-specific arrest of primer extension on single-stranded DNA by an oligonucleotide-minor groove binder conjugate," Proc. Natl. Acad. Sci. USA (1996) 93:3199-3204.					
	437	Agrawal, et al., "Oligodeoxynucleoside Phosphoramidates and Phosphorothioates as Inhibitors of Human Immunodeficiency Virus" Proc. Natl. Acad. Sci. USA, 1988, 85, 7079-7083					
	438	Agarwal, et al., "Synthesis and Enzymatic Properties of Deoxyribooligonucleotides Containing Methyl and Phenylphosphonate Linkages", Nucleic Acid Research 1979, 6, 3009-3024					
	439	Agrawal, S. et al., "Antisense therapeutics: is it as simple as complementary base recognition?," Molecular Med. Today, Vol. 6(2), pages 72-81 (2000)					
	440	Agris, et al., "Inhibition of Vesicular Stomatitis Virus Protein Synthesis and Infection by Sequence-Specific Oligodeoxyribonucleoside Methylphosphonates", Biochemistry 1986, 25, 6268-6275					
	441	Allerson, C.R. et al., abstract of the 227th ACS National Meeting, Anaheim, CA, March 28-April 1, 2004					
	442	Allerson, C.R. et al., "Fully 2'-Modified Oligonucleotide Duplexes with Improved in Vitro Potency and Stability Compared to Unmodified Small Interfering RNA," J. Med. Chem., 2005, 48, 901-904					
	443	Altmann, KH. et al., "Second generation antisense oligonucleotides - inhibition of PKC-alpha and c-RAF kinase expression by chimeric oligonucleotides incorporating 6' -substituted carbocyclic nucleosides and 2' -O-ethylene glycol substituted ribonucleosides," Nucleosides & Nucleotides, 1997, 16(7-9), 917-926					
	444	Altmann, KH., et al., "Second generation of antisense oligonucleotides: from nuclease resistance to biological efficacy in animals," Chimia, 1996, 50, 168-176					
	445	Altmann, K.H., et al., "Second-generation antisense oligonucleotides: structure-activity relationships and the design of improved signal-transduction inhibitors," Biochem. Soc. Trans., 1996, 24, 630-637					
	446	Altschul, S.F. et al., "Basic Local Alignment Search Tool," J. Mol. Biol., 1990, 215, 403-410					
	447	Ambros, V. et al., "A uniform system for MicroRNA annotation," RNA (2003) 9: 277-279					

Examiner	Date	
Signature	Considered	

	Substitute for 1440/PTO			Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STA	STATEMENT BY APPLICANT			First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	21	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS	
448	Ambros, V. et al., "MicroRNAs and Other Tiny Endogenous RNAs in C. elegans, "Curr Biol. (2003) 13: 807-818	
449	Ambros, V. et al., "MicroRNAs: Tiny Regulators with Great Potential," Cell (2001) 107: 823-826	
450	Antopolsky, M. et al., "Peptide-Oligonucleotide Phosphorothioate Conjugates with Membrane Translocation and Nuclear Localization Properties," Bioconjuxate Chem. (1999) 10(4):598-606.	
451	Arar, K. et al., "Synthesis and Antiviral Activity of Peptide-Oligonucleotide Conjugates Prepared by Using Na-(Bromoaceytl)peptides," Bioconjugate Chem. (1995) 6(5):573-577.	
452	Arnott, S., et al., "Optimised parameters for A-DNA and B-DNA," Biochem. & Biophys. Res. Comm., 1972, 47(6), 1504-1510	
453	Asseline, U. et al., "Nucleic acid-binding molecules with high affinity and base sequence specificity: Intercalating agents covalently linked to oligodeoxynucleotides," Proc. Natl. Acad. Sci USA (1984) 81: 3297-3301	
454	Astriab-Fisher et al., "Conjugates of antisense olgonucleotides with the TAT and antennapedia cell-penetrating peptides: effects on cellular update, binding to target sequences and biologic actions," Pharmaceutical Research (2002) 19(6): 744-754	
455	Astriab-Fisher, A. et al., "Antisense Inhibition of P-glycoprotein Expression Using Peptide-Oligonucleotide Conjugates," Biochem. Pharmacol. (2000) 60, 83-90.	
456	Baker, B. F. et al., "Oligonucleotide-europium complex conjugate designed to cleave the 5' cap structure of the ICAM-I transcript potentiates antisense activity in cells," Nucleic Acids Res. (1999) 27(6):1547-1551.	
457	Baker, B.F., et al., "2'-O-(2-methoxy)ethyl-modified anti-intercellular adhesion molecule 1 (ICAM-1) oligonucleotides selectively increase the ICAM-1 mRNA level and inhibit formation of the ICAM-1 translation initiation complex in human umbilical vein endothelial cells," J. Biol. Chem., 1997, 272(18), 11944-12000	
458	Bartel, B. et al., "MicroRNAs: At the Root of Plant Development," Plant Physiol. (2003) 132, 709-717	
459	Bass, B.L., "Double-stranded RNA as a template for gene silencing," Cell, 2000, 101, 235-238	
460	Bayer, E. et al., "A New Support for Polypeptide Synthesis in Columns," Tetrahedron Letters, 1970, 51, 4503-4505	
461	Beaucage et al. "The Functionalization of Oligonucleotides Via Phosphoramidite Derivatives", (1993) Tetrahedron 49(10):1925-1963	
462	Beaucage, S.L. et al., "Deoxynucleoside Phosphoramidites-A New Class of Key Intermediates for Deoxypolynucleotide Synthesis,", Tetrahedron Letts., 1981, 22, 1859-1862	

Examiner	Date	
Signature	Considered	

	1.4.40/DTO			Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT			ANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	22	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS	
463	Biggadike, et al., "Short convergent route to homochiral carbocylic 2'-deoxynucleosides and carbocyclic robonucleosides", J. Chem. Soc. Chem. Commun. 1987, 1083-1084	
464	Bollig, F. et a]., "Affinity purification of ARE-binding proteins identifies poly(A)-binding protein 1 as a potential substrate in MK2-induced mRNA stabilization," Biochem. Bioophys. Res. Commun. (2003) 301: 665-670	
465	Bongartz, JP. et al., "Improved biological activity of antisense oligonucleotides conjugated to a fusogenic peptide," Nucleic Acids Res. (1994) 22(22):4681-4688.	
466	Bonora, G. M. et al., "Antisense activity of an anti-HIV oligonucleotide conjugated to linear and branched high molecular weight polyethylene glycols," Farmaco (1998) 53:634-637.	
467	Bonora, G. M. et al., "Biological Properties of Antisense Oligonucleotides Conjugated to - Different High-Molecular Mass Poly(Ethy1en Glycols)," Nucleosides Nucleotides (1999) 18(6&7):1723-1725	
468	Bonora, G.M., et al., "A liquid-phase process suitable for large-scale synthesis of phosphorothioate oligonucleotides," Organic Process Res. & Develop., 2000, 225-231	
469	Borer, et al., "Stability of ribonucleic acid double-stranded helices," J. Mol. Biol., 1974, 86, 843-853	
470	Braasch et al., "Antisense inhibition of gene expression in cells by oligonucleotides incorporating locked nucleic acids: effect of mRNA target sequence and chimera design," Nucleic Acids Research, 2002, 30, 5160-5167	
471	Braasch, D.A. et al., "Locked nucleic acid (LNA): fine-tuning the recognition of DNA and RNA," Chem Biol, 2001, 8, 1-7	
472	Braasch, D.A. et al., "RNA Interference in Mammalian Cells by Chemically-Modified RNA," Biochemistry, 2003, 42, 7967-7975	
473	Braasch, D.A., et al., "Novel antisense and peptide nucleic acid strategies for controlling gene expression," Biochemistry, April 9, 2002, 41(14), 4503-4510	
474	Branda et al., "Amplication of antibody production by phosphorothioate oligodeoxynucleotides," J. Lab. Clin. Med., 1996, 128, 329-338	
475	Branden, L. J. et al., "A peptide nucleic acid-nuclear localization signal fusion that mediates nuclear transport of DNA," Nature Biotech (1999) 17:784-787.	
476	Brantl, S., "Antisense-RNA regulation and RNA interference," Biochimica et Biophysica Acta, 2002, 1575, 15-25	
477	Brazma, A., et al., "Gene expression data analysis," FEBS Lett., 2000, 480, 17-24	
478	Brill, et al., "Synthesis of Oligodeoxynucleoside Phosphorodithioates Via Thioamidites", J. Am. Chem. Soc. 1989, 111, 2321-2322	

Examiner	Date	
Signature	Considered	

	1.4.10/DTO			Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		I DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	23	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS	
479	Brown-Driver et al., "Inhibition of Translation of Hepatitis C Virus RNA by 2'-Modified Antisense Oligonucleotides," Antisense Nucleic Acid Drug Dev. (1999) 9(2): 145-154	
480	Buhr, C.A. et al., "Oligodeoxynucleotides containing C-7 propyne analogs of 7-deaza-2'-deoxyguanosine and 7-deaza-2'-deoxyadenosine," Nucleic Acids Research, 1996, 24(15), 2974-2980	
481	Butke, et al., "Facile synthesis of 2'amino-2deoxynucleoside from the corresponding arabino derivative," Nucleic Acid Chemistry, 1986, Part Three, 149-152	
482	Butler, M. et al., "Specific Inhibition of PTEN Expression Reverses Hyperglycemia in Diabetic Mice," Diabetes, 2002, 51, 1028-1034	
483	Caplen et al., "dsRNA-mediated gene silencing in cultured Drosophila cells: a tissue culture model for the analysis of RNA interference," GENE (2000) 252: 95-105	
484	Caplen, N.J., et al., "Specific inhibition of gene expression by small double-stranded RNAs in invertebrate and vertebrate systems," PNAS, 2001, 98(17), 9742-9747	
485	Carmell, M.A. et al., "the argonaute family: tentacles that reach into RNAi, developmental control, stem cell maintenance, and tumorigenesis," Genes and Development, 2002, 16, 2733-2742	
486	Carulli, J.P., et al., "High throughput analysis of differential gene expression," J. Cellular Biochem. Suppl., 1998, 30(31), 286-296	
487	Caruthers, M., "Synthesis of Oligonucleotides and Oligonucleotide Analogues", in "Oligonucleotides. Antisense Inhibitors of Gene Expression.", J.S. Cohen, Ed., CRC Press, Inc., 7-24, (1989)	
488	Castle, et al., "Imidazo[4, 5-D]pyridazines. I. Synthesis of 4,7-disubstituted derivatives", Journal of Organic Chemistry, 1958, 23, 1534-1538	
489	Cazalla, D. et al., "Nuclear Export and Retention Signals in the RS Domain of SR Proteins," Mol. Cell. Biol. (2002) 22(19):6871-6882.	
490	Cazenave, C. et al., "Enzymatic amplification of translation inhibition of rabbit β-globin mRNA mediated by anti-messenger oligodeoxynucleotides covalently linked to intercalating agents", Nucl. Acids Res., 1987, 15, 4717-4736	
491	Celis, J.E., et al., "Gene expression profiling: monitoring transcription and translation production using DNA microarrays and proteomics," FEBS Lett., 2000, 480, 2-16	
492	Cerutti, H., "RNA interference: traveling in the cell and gaining functions?" Trends in Genetics (2003) 19(1): 39-46	
493	Chaloin, L. et al., "Design of Carrier Peptide-Oligonucleotide Conjugates with Rapid Membrane Translocation and Nuclear Localization Properties," Biochem. Biophys. Res. Commun. (1998) 243:601-608	

Examiner	Date	
Signature	Considered	

0.1.17.1.6.4440/PTO				Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	24	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS
494	Chaput, J.C., et al., "DNA polymerase-mediated DNA synthesis on a TNA template," J. Am. Chem. Soc., 2003, 125, 856-857
495	Chen and Wu, "Studies on Fluoroalkylation and Fluroalkoxylation. Part 33. Direct Trifluoromethylation of Aryl Halides with Fluorosulphonyldifluoromethyl lodide in the Presence of Copper: an Electron Transfer Induced Process," J. Chem. Soc., Perkin Transactions, 1989, 1, 2385-2387.
496	Chiang et al., "Antisense Oligonucleotides Inhibit Intercellular Adhesion Molecule 1 Expression by Two Distinct Mechanisms," J. Biol. Chem., 1991, 266, 18162-18171
497	Chirila, T.V. et al., "The use of synthetic polymers for delivery of therapeutic antisense oligodeoxynucleotides," Biomaterials, Vol. 23(2), pages 321-342 (2002)
498	Chiu et al., "siRNA function in RNAi: a chemical modification analysis," RNA, 2003, 9, 1034-1048
499	Chiu, YL. et al., "RNAi in human cells: basic structural and functional features of small interfering RNA," Molecular Cell, September 2002, 10, 549-561
500	Chladek, et al., "Facile Synthesis of 2'Amino-2'Deoxyadenosine," J. Carbohydtrates, Necleosides & Nucleotides, 1980, 7, 63-75.
501	Choung, S. et al., "Chemical modification of siRNAs to improve serum stability without loss of efficacy," Biochemical and Biophysical Research Communications, 2006, 342, 919-927
502	Christofferson et al., "Ribozymes as human therapeutic agents", J. Med. Chem., 1995, 38(12), 2023-2037
503	Chun-Nam Lok et al., "Potent gene-specific inhibitory properties of mixed backbone antisense oligonucleotides comprised of 2' -deoxy-2' -fluoro-D-arabinose and 2' -deoxyribose nucleotides," Biochemistry, 2002, 41, 3457-3467
504	Cogoni, C. et al., "Post-transcriptional gene silencing across kingdoms," Curr. Opin. Genet Dev., 2000, 10(6), 638-643
505	Cohen , G. L. et al., "Sequence Dependent Binding of cis-Dichlorodiamrnineplatinum(II) to DNA," J. Am. Chem. Soc. (1980) 102(7), 2487-2488.
506	Constant et al., "Heterodimeric Molecules Including Nucleic Acid Bases and 9-Aminoacridine Spectroscopic Studies, Conformations, and Interactions with DNA", Biochemistry, 1988, 27, 3997-4003
507	Conte, M.R., et al., "Conformational properties and thermodynamics of the RNA duplex r(CGCAAAUUUGCG)2: comparison with the DNA analogue d(CGCAAATTTGCG)2," Nucleic Acids Res., 1997, 25(13), 2627-2634
508	Copy of PCT International Search Report dated January 24, 2005 (PCTUS03/35087)
 509	Copy of the PCT International Search Report dated August 13, 2004 (PCT/US03/35072)

Date Considered

Examiner Signature

	1440/PTO	_		Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	25	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS
510	Copy of the PCT International Search Report dated August 2, 2004 (PCT/US03/35068)
511	Copy of the PCT International Search Report dated August 23, 2004 (PCT/US03/35063)
512	Copy of the PCT International Search Report dated December 1, 2003 (PCT/US03/19043)
513	Corey, D. R. et al., "Generation of a Hybrid Sequence-Specific Single-Stranded Deoxyribonuclease," Science (1987) 238:1401-1403.
514	Corey, D. R. et al., "Sequence-Selective Hydrolysis of Duplex DNA by an Oligonucleotide- Directed Nuclease," J. Am. Chem. Soc. (1989) 111(22):8523-8525.
515	Corey, D. R., "48000-fold Acceleration of Hybridization by Chemically Modified Oligonucleotides," J. Am. Chem. Soc. (1995) 117(36):9373-9374.
516	Cornell, W. D. et al., "A Second Generation Force Field for the Simulation of Proteins, Nucleic Acids, and Organic Molecules," J. Am. Chem. Soc., 1995, 117, 5179-5197
517	Cossum, P.A. et al., "Disposition of the 14C-Labeled Phosphorothioate Oligonucleotide ISIS 2105 after Intravenous Administration to Rats," J. Pharmacol. Exp. Ther., 1993, 267(3), 1181-1190
518	Couzin, J., "Small TNAs Make Big Splash," Science (2002) 298: 2296-2297
519	Crawford, J.M., "Role of Vesicle-Mediated Transport Pathways in Hepatocellular Bile Secretion," Semin. Liver Dis., 1996, 16(2), 169-189
520	Crooke, S.T., Antisense Research & Application, Chapter1, Pages 1-50, Publ. Springer-Verlag, Ed. S.T. Crooke (1998).
521	Cummins, L.L. et al., "Characterization of fully 2'modified oligoribonucleotide hetero- and homoduplex hybridization and nuclease sensitivity," Nucleic Acids Research, 1995, 23(11), 2019-2024
522	Czauderna, F., et al., "Structural variations and stabilizing modifications of synthetic siRNAs in mammalian cells," Nucleic Acids Res., 2003, 31(11), 2705-2716
523	Dahl, B.H. et al., "A Highly Reactive, Odourless Substitute for Thiphenol/Triethylmaine as a Deprotection Reagent in the Synthesis of Oligonucleotides and their Analogues," Acta Chem. Scand., 1990, 44, 639-641
524	Damha, et al., "Solution and solid phase chemical synthesis of arabinonucleotides", Can J. Chem., 1989, 831-839
525	Dande, P. et al., Abstract from The 227th ACS National Meeting, Anaheim, CA, March 28-April 1, 2004
526	De las Heras, et al., "3'-C-Cyano-3'-Deoxythymidine," Tetrahedron Letters, 1988, 29, 941-944

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
		I DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	eets as necessary)		Examiner Name	Sean McGarry	
Sheet	26	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS
527	Dellinger, D.J. et al., "Solid-Phase Chemical Synthesis of Phosphonoacetate and Thiophosphonoacetate Oligodexynucleotides," J. Am. Chem. Soc., 2003, 125(4), 940-950
528	Denny, W.A., "DNA-intercalating ligands as anti-cancer drugs: prospects for future design," Anti-Cancer Drug Design, 1989, 4, 241-263
529	Dignam, et al., "Accurate transcription initiation by RNA polymerase II in a soluble extract from isolated mammalian nuclei," Nucleic Acids Res., 1983, 11, 1475-1489
530	Divakar, et al., "Approaches to the Synthesis of 2'-Thio Analogues of Pyrimidine Ribosides", J. Chem. Soc., Perkins Trans., I, 1990, 969-974
531	Divakar, et al., "Reaction Between 2,2'-Anhydro-1-β-D-arrabinofuranosyluracil and Thiolate lons", J. Chem. Soc., Perkins Trans. I, 1982, 1625-1628
532	Dreyer, et al., "Sequence-specific cleavage of single-stranded DNA: Oligodeoxynucleotide-EDTA-Fe(II)", Proc. Natl. Acad. Sci. USA, 1985, 82, 968-972
533	Duff, R. J. et al., "[17] Intrabody Tissue-Specific Delivery of Antisense Conjugates in Animals: Ligand-Linker-Antisense Oligomer Conjugates," Methods Enzymol. (2000) 313:297-321.
534	Eckstein, et al., "Polynucleotides Containing 2'Chloro-2'Deoxyribose", Biochemistry, 1972, 11, 4336-4344
535	Eddy, S.R., "Non-Coding RNA Genes and the Modern RNA World," Nature Rev. Genetics (2001) 2: 919-929
536	Efimov, V. A. et al., "Synthesis of Polyethylene Glycol - Oligonucleotide Conjugates," Bioorg. Khim. (1993) 19(8):800-804.
537	Egli, M. et al., "RNA Hydration: A Detailed Look," Biochemistry, 1996, 35, 8489-8494
538	Elayadi, A.N. et al., "Application of PNA and LNA oligomers to chemotherapy," Curr. Opin. Investig. Drugs, 2001, 2(4), 558-561
539	Elbashir S.M., "Duplexes of 21-nucleotide RNAs mediate RNA interference in cultured mammalian cells," Nature, 2001, 411, 494-498
540	Elbashir, S.M., "RNA interference is mediated by 21- and 22-nucleotide RNAs," Genes & Devel., 2001, 15, 188-200
541	Elmén, J. et al., "Locked nucleic acid (LNA) mediated improvements in siRNA stability and functionality," Nucleic Acids Res. 2005, 33(1), 439-447
542	EP Supplementary Search Report for EP 03716922 dated May 12, 2006
543	Faria, M. et al., "Phosphoramidate oligonucleotides as potent antisense molecules in cells and in vivo," Nature Biotech., 2001, 19, 40-44
544	Fazakerley, G.V., et al., "A→Z transition in the synthetic hexanucleotide (dCdGfl)3," FEBS, 1985, 182(2), 365-369

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	27	of	47	Attorney Docket Number	ISIS-5027	

NON PATENT LITERATURE DOCUMENTS						
545	Fedoroff, O.Y. et al., "Structure of a DNA:RNA Hybrid Duplex," J. Mol. Biol., 1993, 233, 509-523					
546	Fire et al., "RNA-triggered gene silencing," TIG (1999) 15(9): 358-363					
547	Fire et al., Nature, 1998, 391, 806-811					
548	Firestone, R. A., "Low-Density Lipoprotein as a Vehicle for Targeting Antitumor Compounds to Cancer Cells," Bioconjugate Chern. (1994) 105-113					
549	Flanagan, W. M. et al., "A cytosine analog that confers enhanced potency to antisense oligonucleotides," Proc. Natl. Acad. Sci. USA, Mar. 1999, 96, 3513-3518					
550	Flanagan, W.M. et al., "Cellular penetration and antisense activity by a phenoxazine-substituted heptanucleotide," Nature Biotechnol. (1999) 17(1): 48-52					
551	Fluiter, K. et al., "In vivo tumor growth inhibition and biodistribution studies of locked nucleic acids (LNA) antisense oligonucleotides," Nucleic Acids Res., 2003, 31(3), 953-962					
552	Fox, et al., "Nucleosides. XVIII. Synthesis of 2'-Fluorothymidine, 2'-Flurodeoxyuridine, and Other 2'-Halogeno-2'-Deoxy Nucleosides 12", J Org. Chem., 1964, 29, 558-564					
553	Francis, A.W. et al., "Probing the Requirements for Recognition and Catalysis in Fpg and MutY with Nonpolar Adenine Isosteres," J. Am. Chem. Soc. (2003) 125(52): 16235-16242					
554	Fraser, A., et al., "Synthesis and conformational properties of 2'-deoxy-2'-methylthiopyrimidine and -purine nucleosides:potential antisense applications," J. Heterocycl. Chem., 1993, 30, 1277-1287					
555	Fraser, A.G. et al., "Functional genomic analysis of C. elegans chromosome 1 by systemic RNA interference," Nature, 2000, 408, 325-330					
556	Freier, S. M. et al., "The ups and downs of nucleic acid duplex stability: structure–stability studies on chemically-modified DNA:RNA duplexes," Nucleic Acids Research, 1997, 25(22), 4429-4443					
557	Freskos, "Synthesis of 2'Deoxypyrimidine Nucleosides Via Copper (I) Iodine Catalysis," Nucleosides & Nucleotides, 1989, 8, 1075, 1076					
558	Frieden, M. et al., 'Expanding the design horizon of antisense oligonucleotides with alpha-L-LNA," Nucleic Acids Res., 2003, 31(21), 6365-6372					
559	Fromageot, H.P.M. et al., "The Synthesis of Oligonucleotides," Tetrahedron, 1967, 23, 2315-2331					
560	Fuchs, B. et al., "Identification of Differentially Expressed Genes by Mutually Subtracted RNA Fingerprinting," Anal. Biochem., 2000, 286, 91-98					
561	Gaffney, et al., "A New Strategy for the Protection of eoxyguanosine During Oligonucleotide Synthesis," Tetrahedron Letters, 1982, 23, 2257-2260					

Examiner	Date	
Signature	Considered	

0 L ("L L L AAAO/DTO				Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	28	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS						
562	Gait, M.J. et al., "Application of chemically synthesized RNA," RNA: Protein Interactions (1998) Smith (ed.), pp. 1-36						
563	Gait, M.J., "Oligoribonucleotides, Antisense Research and Applications, 1993, Crooke, S.T. and Lebleu, B. (eds.), CRC Press, Boca Raton, pp. 289-301						
564	Gallo, M. et al., "2'-C-Methyluridine phosphoramidite: a new building block for the preparation of RNA analogues carrying the 2'-hydroxyl group," Tetrahedron, 2001, 57(27), 5707-5713						
565	Gao, J. et al., "Expanded-Size Bases in Naturally Sized DNA: Evaluation of Steric Effects in Watson-Crick Pairing," J. Am. Chem. Soc. (2004) 126(38): 11826-11831						
566	Geary, R.S. et al., "Pharmacokinetic Properties of 2'-O-(2-Methoxyethyl)-Modified Oligonucleotide Analogs in Rats," J. Pharmacol. Exp. Therap., 1998, 296(3), 890-897						
567	Going, J.J., et al., "Molecular pathology and future developments," Eur. J. Cancer, 1999, 35(14), 1895-1904						
568	Gonzalez, C. et al., "Structure and Dynamics of a DNA-RNA Hybrid Duplex with a Chral Phosphorothioate Moiety: NMR and Molecular Dynamics with Conventional and Time-Averaged Restraints," Biochemistry, 1995, 34, 4969-4982						
569	Gorlach, M. et al., "The rnRNA Poly(A)-Binding Protein: Localization, Abundance, and RNABinding Specificity," Exp. Cells Res. (1994) 211:400-407						
570	Graham, et al., "Tritium Labeling of Antisense Oligonucleotides by Exchange with Tritiated Water," Nucleic Acids. Res., 1993, 16, 3737-3743						
571	Graham, M.J. et al., "In Vivo Distribution and Metabolism of a Phosphorothioate Oligonucleotide within Rat Liver after Intravenous Administration," J. Pharmacol. Exp. Therap., 1998, 286(1), 447-458						
572	Gravert, D.J., et al., "Organic synthesis on soluble polymer supports," Chem. Rev., 1997, 97, 489-509						
573	Griffey, R.H. et al., "2'-O-Aminopropyl Ribonucleotides: A Zwitterionic Modification that Enhances the Exonuclease Resistance and Biological Activity of Antisense Oligonucleotides," J. Med. Chem., 1996, 39(26), 5100-5109						
574	Griffin, B.E. et al., "The Synthesis of Oligoribonucleotides," Tetrahedron, 1967, 23, 2301-2313						
575	Grishok, A. et al., "Genetic Requirements for Inheritance of RNAi in C. elegans," Science, 2000, 287, 2494-2497						
576	Grünweller, A. et al., "Comparison of different antisense strategies in mammalian cells using locked nucleic acids, 2'-O-methyl RNA, phosphorothioates and small interfering RNA," Nucleic Acids Research, 2003, 31(12), 3185-3193						
577	Gryaznov, S. et al., "Oligodeoxynucleotide N3'P5' Phosphoramidates: Synthesis and Hybridization Properties," J. Am. Chem. Soc., 1994, 116(7), 3143-3144						

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT			ANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	29	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS						
578	Guckian, K.M. et al., "Structure and Base Pairing Properties of a Replicable Nonpolar Isostere for Deoxyadenosine," J Org Chem (1998) 63(26);9652-9656						
579	Guillerm, D. et al., "Synthesis of 4'-fluoroadenosine as an inhibitor of S-adenosyl-L-homocysteine hydrolase," Bioorganic & Medicinal Chemistry Letters, 1995, 5(14), 1455-1460						
580	Guo, S. et al., "par-1, a Gene Required for Establishing Polarity in C. elegans Embryos, Encodes a Putative Ser/Thr Kinase That is Asymmetrically Distributed," Cell, 1995, 81(4), 611-620						
581	Gura, T., "A silence that speaks volumes," Nature, 2000, 404, 804-808						
582	Guschlbauer, et al., "Nucleoside conformation is Determined by the Electronegativity of the Sugar Substituent," Nucleic Acids Res., 1980, 8, 1421-1433						
583	Guschlbauer, W. et al., "Poly-2'-deoxy-2'-fluoro-cytidylic acid: enzymatic synthesis, spectroscopic characterization and interaction with poly-inosinic acid," Nucleic Acid Research, 1977, 4(6),1933-1943						
584	Guschlbauer, W., et al., "Use of 2'-deoxy-2'-fluoro-necleosides in the study of polynucleotide conformation: a progress report," Nucleic Acid Research Symposium Series, 1982, 11,113-116						
585	Gutierrez, A.J. et al., "Antisense Gene Inhibition by C-5 Substituted Deoxyuridine-Containing Oligodeoxynucleotides," Biochemistry, 1997, 36(4), 743-748						
586	Guzaev, A. et al., "Conjugation of Oligonucleotides Via an Electrophilic Tether: N-Chloroacetarnidohexyl Phosphoramidite Reagent," Bioorg. Med. Chem. lett . (1998) 8:3671-3676.						
587	Hakimelahi, G.H. et al., "High Yield Selective 3'-Silylation of Ribonucleosides," Tetrahedron Lett., 1981, 22(52), 5243-5246						
588	Hall, J. et al., "Efficient sequence-specific cleavage of RNA using novel europium complexes conjugated to oligonucleotides," Chem. Biol. (1994) 1(3):185-190.						
589	Hamada et al., "Effects on RNA Interference in Gene Expression (RNAi) in Cultured Mammalian Cells of Mismatches and the Introduction of Chemical Modifications at the 3'Ends of siRNAs," Antisense and Nucleic Acid Drug Development (2002) 12:301-309						
590	Hansske, et al., "2'and 3'-ketonucleosides and their arabino and XYLO reduction products," Tetrahedron, 1984, 40, 125-135						
591	Hariton-Gazal, E. et al., "Targeting of Nonkaryophilic Cell-Permeable Peptides into the Nuclei of Intact Cells by Covalently Attached Nuclear Localization Signals," Biochemistry (2002) 41(29):9208-9214.						
592	Harry O'Kuru, R.E. et al., "A Short, Flexible Route toward 2'-C-Branched Ribonucleosides," J. Org. Chem., 1997, 62(6), 1754-1759						

Examiner	Date	
Signature	Considered	

	1.4.40/DTO			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STA	LEMENT E	BY APPLIC	ANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	30	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS						
593	Heasman, J., "Morpholino Oligos: Making Sense of Antisense?" Dev. Biol., 2002, 243, 209-214						
594	Henderson, B. R. et al., "A Comparison of the Activity, Sequence Specificity, and CRM1-Dependence of Different Nuclear Export Signals," Exp. Cell Res. (2000) 256:213-224.						
595	Hertel, et al., "Synthesis of 2-deoxy-2,2-difluoro-D-ribose and 2-deoxy-2,2-difluoro-D-ribofuranosyl nucleosides," J. Org. Chem., 1988, 53, 2406-2409.						
596	Hill, F. et al., "Polymerase recognition of synthetic oligodeoxyribonucleotides incorporating degenerate pyrimidine and purine bases," Proc. Natl. Acad. Sci. USA, 1998, 95, 4258-4263						
597	Hoffman, K., "Imidazole and its Derivatives" in The Chemistry of Heterocyclic Compounds, Weissberger, A., Ed.,Interscience Publishers, Inc., New York, 1953, 447						
598	Holen, T., et al., "Similar behaviour of single-strand and double-strand siRNAs suggests they act through a common RNAi pathway," Nucleic Acids Res., 2003, 31(9), 2401-2407						
599	Hornbeck, P. et al., Enzyme-Linked Immunosorbet Assays (ELIASE)," Curr. Protocols Mol. Biol., 1991, John Wiley & Sons, pp. 11.2.1-11.2.22						
600	Hornung, V. et al., "Sequence-specific potent induction of IFN-a by short ineterfering RNA in plasmacytoid dendritic cells through TLR7," Nature Med., 2005, 11(3), 263-270						
601	Horton, N. C. et al., "The Structure of an RNA/DNA Hybrid: A Substrate of the Ribonuclease Activity of HIV-1 Reverse Transcriptase," J. Mol. Biol., 1996, 264, 521-533						
602	Huang, L. et al., "Oligonucleotide conjugates of Eu(III) tetraazamacrocycles with pendent alcohol and amide groups promote sequence-specific RNA cleavage," J Biol Inorg. Chem (2000) 5:85-92.						
603	Huh, N. et al., "Design, Synthesis, and Evaluation of Mitomycin-Tethered Phosphorothioate Oligodeoxynucleotides," Bioconjugate Chem. (1996) 7:659-669.						
604	Ikehara, et al, "Studies of Nucleosides and Nucleotides-LXV' Purine Cyclonucleosides-26 A Versatile Method for the Synthesis of Purine O-Cyclo-Bucleosides. The First Synthesis of 8,2'Anhydro-8-Oxy 9-B-D-Arabinofuranosylguanine," Tetrahedron, 1975, 31, 1369-1372						
605	Ikehara, et al, "Studies of Nucleosides and Nucleotides-LXXXVII. 1, Purine Cyclonucleosides. XLII. Synthesis of 2'deoxy-2'fluorofunaosine," Chem. And Pharm. Bull., 1981, 29, 1034-1038.						
606	Ikehara, et al. "Purine cyclonucleosides. (43). Synthesis and properties of 2'halogen-2'deoxyguanosines 1," Chem and Pharm Bull., 1981, 29, 3281-3285						
607	Ikehara, et al., "A Linear Relationship Between Electronegativity of 2'-Substituents and Conformation of Adenine Nucleosides," Tetrahedron Letters, 1979, 42, 4073-4076						
608	Ikehara, et al., "Improved Synthesis of 2'-fluoro-2'deoxyadenosine and Synthesis and Carbon-13 NMR Spectrum of its 3',5'-cyclic Phosphate Derivative," Nucleosides & Nucleotides, 1983, 2, 373-385						

Examiner	Date	
Signature	Considered	

	1440/DT0			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STATEMENT BY APPLICANT				First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	31	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS
609	Ikehara, et al., "Polynucleotides. L. synthesis and properties of poly (2'chloro-2'-deoxyadenylic acid) and poly (2'-bromo-2'-deoxyadenylic acid)", Nucleic Acids Res., 1978, 4, 4249-4260
610	Ikehara, et al., "Polynucleotides. LII. Synthesis and properties of poly (2'-deox-2'-fluoroadenylic acid)," Nucleic Acids Research, 1978, 5, 1877-1887
611	Ikehara, et al., "Polynucleotides. LVI. Synthesis and Properties of Poly(2'-deoxy-2'-fluoroinosinic Acid)", Nucleic Acids Res., 1978, 5, 3315-3324
612	Ikehara, et al., "Purine 8-Cyclonucleosides," Accts. Chem Res., 1969, 2, 47-53
613	Ikehara, et al., "Studies of Nucleosides and Nucleotides-LXXIV1 Purine Cyclonucleosides34 A New Method for the Synthesis of 2'-substituted 2'-deoxyadenosines," Tetrahedron, 1978, 34, 1133-1138
614	Ikehara, et al., "Studies of Nucleosides and Nucleotides-LXXXII. 1 Cyclonucleosides. (39). 2 Synthesis and properties of 2'halogen-2'-deoxyadenosines," Chem. Pharm. Bull., 1978, 26, 2449-2453
615	Ikehara, M., "2'-substituted 2'-deoxypurineucleotides their conformation and properties," Heterocycles, 1984, 21(1), 75-90
616	Imazawa, et al., "Nucleosides and nucleotides. XII.1) Synthesis and properties of 2'-deoxy-2'-mercaptouridine and its derivates", Chem. Pharm. Bull., 1975, 23, 604-610
617	Inoue et al., "Sequence dependent hydrolysis of RNA using modified oligonucleotide splints and Rnase H", FEBS Lett., 1987, 215(2), 327-330
618	Inoue, et al., "Synthesis and hybridization studies on two complementary nona(2'-O-methyl) ribonucleotides", Nucleic Acid Res., 1987, 15, 6131-6148
619	International Search Report dated March 24, 2005 for International Application No. PCT/US03/35088
620	International Search Report dated November 18, 2004 for International Application No. PCT/US03/29294
621	Jacobson, K.A. et al., "Methanocarba Analogues of Purine Nucleosides as Potent and Selective Adenosine Receptor Agonists," J. Med. Chem., 2000, 43(11), 2196-2203
622	Jäger, A. et al., "Oligonucleotide N-alkylphosphoramidates: Synthesis and binding to polynucleotides", Biochemistry 1988, 27, 7237-7246
623	Janik, B., et al., "Synthesis and Properties of Poly 2'-Fluoro-2'-Deoxyuridylic Acid," Biochem. Biophys. Res. Comm., 1972, 46(3), 1153-1160
624	Jarvi, et al., "Synthesis and biological evaluation of dideoxunucleosides containing a difluoromethylene unit", Nucleosides & Nucleotides, 1989, 8, 1111-1114
625	Jaschke, A. et al., "Synthesis and properties of oligodeoxyribonucleotide-polyethyleneg lycol conjugates," Nucleic Acids Res. (1994) 22(22):4810-4817.

Examiner	Date	
Signature	Considered	

	1.4.40/DTO			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STA	LEMENT E	BY APPLIC	ANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	32	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS	
626	Jayaraman, et al., "Selective Inhibition of Escherichia Coli Protein Synthesis and Growth by Nonionic Oligonucleotides Complementary to the 3' end of 16S rRNA", Proc. Natl. Acad. Sci. USA 1981, 78(3), 1537-1541	
627	Jen et al., "Suppression of Gene Expression by Targeted Disruption of Messenger RNA: Available Options and Current Strategies," Stem Cells, 2000, 18, 307-319	
628	Jones, et al., "4'-substituted nucleosides. 5. hydroxymethylation of nucleoside 5'-aldehydes", J. Org. Chem., 1979, 44, 1309-1317	
629	Jones, et al., "Transient protection: Efficient one-flask synthesis of protected deoxynucleosides", J. Am. Chem. Soc., 1982, 104, 1316-1319	
630	Jones, L.J. et al., "RNA Quantitation by Fluorescence-Based Solution Assay: RiboGreen Reagent Characterization," Anal. Biochem., 1998, 265, 368-374	
631	Jones, S.S. et al., "Migration of t-Butyldimethylsilyl Protecting Groups," J.C.S. Perkin 1, 1979, 2762-2764	
632	Jorgensen. R. A. et al., "Chalcone synthase cosuppression phenotypes in petunia flowers: comparison of sense vs. antisense constructs and single-copy vs. complex T-DNA sequences," Plant Mol. Biol., 1996, 31(5), 957-973	
633	Juby, C. D. et al., "Facile Preparation of 3'0ligonucleotide-Peptide Conjugates," Tetrahedron Letters (1991) 32(7):879-882.	
634	Jungblut, P.R., et al., "Proteomics in human disease: cancer, heart and infectious diseases," Electrophoresis, 1999, 20, 2100-2110	
635	Jurecic, R., et al., "Long-distance DD-PCR and cDNA microarrays," Curr. Opin. Mocrobiol., 2000, 3, 316-321	
636	Kabanov, A.V.,"A new class of antivirals: antisense olgonucleotides combined with a hydrophobic substituent effectively inhibit influenza virus reproduction and synthesis of virus-specific proteins in MDCK cells", FEBS Letts., 1990, 259, 327-330	
637	Kawasaki, H/ et al., "Hesl is a target of MicroRNA-23 during retinoic-acid-induced neuronal differentation of NT2 cells," Nature (2003) 423: 838-842	
638	Khurshid et al., "The unique conformational stability of poly 2'-O-Ethyladenylic Acid," FEBS Letters, 1972, 28(1), 25	
639	Khvorova, A. et al., "Functional siRNAs Exhibit Strand Bias," Cell, 2003, 115(2), 209-216	
640	Kiaris, H. et al., "Antagonists of Growth Hormone-Releasing Hormone Inhibit the Growth of U-87MG Human Gliobastoma in Nude mice," Neoplasia, 2000, 2(3), 242-250	
641	Kielanowska et al., "Preparation and properties of poly 2'-O-ethylcytidylic acid," Nucl. Acids Res., 1976, 3(3), 817-824	

Examiner	Date	
Signature	Considered	

	1.4.40/DTO			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STA	LEMENT E	BY APPLIC	ANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	33	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS	
642	Kingston, R.E. et al., "Calcium Phosphate Transfection", Current Protocols in Neuroscience, 1997, Supplement 1, A.1C.1 – A.1C.8	
643	Klopffer, A.E. et al., "Synthesis of 2'-Aminoalkyl-Substituted Fluorinated Nucleobases and Their Influence on the Kinetic Properties of Hammerhead Ribozymes," ChemBioChem (2004) 5: 707-716	
644	Klopffer, A.E. et al., "The effect of universal fluorinated nucleobases on the catalytic activity of ribozymes," Nucleosides Nucleotides Nucleic Acids (2003) 22(5-8): 1347-1350	
645	Knorre, et al., "Complementary-Addressed Sequence-Specific Modification of Nucleic Acids", Progress in Nucleic Acid Research and Molecular Biology 1985, 32, 291-321	
646	Koole, et al., "Synthesis of phosphate-methylated DNA fragments using 9-fluorenylmethoxycarbonyl as transient base protecting group", J. Org. Chem., 1989, 54, 1657-1664	
647	Koshkin, A.A., et al., "LNA (locked nucleic acid): an RNA mimic forming exceedingly stable LNA:LNA duplexes," J. Am. Chem. Soc., 1998, 120, 13252-13253	
648	Koshkin, A.A., et al., "LNA (locked nucleic acids): synthesis of the adenine, cytosine, guanine, 5-methylcytosine, thymine and uracil bicyclonucleoside monomers, oligomerisation, and unprecedented nucleic acid recognition," Tetrahedron, 1998, 54, 3607-3630	
649	Kraynack, B.A. et al., "Small interfering RNAs containing full 2'-O-methylribonucleotide-modified sense strands display Argonaute2/elF2C2-dependent activity," RNA, 2006, 12, 163-176	
650	Krieg, A. M. et al., "Uptake of Oligodeoxyribonucleotides by Lymphoid Cells Is Heterogeneous and Inducible," Antisense Research and Development (1991) 1:161-171.	
651	Kroschwitz, J.I. (Ed.), The Concise Encyclopedia of Polymer Science and Engineering, John Wiley & Sons, 1990, 858-859	
652	Krug, A., et al., "Synthesis of oligonucleotide probes containing 2'-deoxy-2'-fluoronucleosides for cleavage of RNA by RNase H," Biomed. Biochem. Acta, 1990, 49, 161-166	
653	Krug, A., et al., "The behaviour of 2'-deoxy-2'-fluorouridine incorporated into oligonucleotides by the phosphoramidite approach," Nucleosides & Nucleotides, 1989, 8(8), 1473-1483	
654	Kuijpers, W. H. A. et al., "Specific Recognition of Antibody-Oligonucleotide Conjugates by Radiolabeled Antisense Nucleotides: A Novel Approach for Two-Step Radioimmunotherapy of Cancer," Bioconjugate Chem. (1993) 4(1):94-102.	
655	Kumar, R., et al., "The first analogues of LNA (locked nucleic acids): phosphorothioate-LNA and 2'-thio-LNA," Bioorg. Med. Chem. Lett., 1998, 8, 2219-2222	
656	Kurchavov, N.A., et al., "A new phosphoramidite reagent for the incorporation of diazaphenoxazinone nucleoside with enhanced base-pairing properties into oligodeoxynucleotides," Nucleosides and Nucleotides, 1997, 16, 1837-1846	

Examiner	Date	
Signature	Considered	

	1.1.10/DTO			Complete if Known		
Substitute for 1449/PTO				Application Number	10/078,949	
		I DISCLOS		Filing Date	02-20-2002	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	eets as necessary)		Examiner Name	Sean McGarry	
Sheet	34	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS							
	657	Kurreck, J., "Antisense technologies, Improvement through novel chemical modifications," Eur. J. Biochem., 2003, 270(8), 1628-1644						
	658	Kusmierek et al., "Alkyation of cytidine-5'-phosphate: Mechanisms of alkylation, influence of O'-alkylation on susceptibility of pyrimidine nucleotides to some nucleolytic enzymes, and synthesis of 2'-O-alkyl polynucleotides," ACTA Biochim. Polonica, 1973, 20(4), 365-381						
	659	Lacerra, G., et al., "Restoration of hemoglobin a synthesis in erythroid cells from peripheral blood of thalassemic patients," Proc. Natl. Acad. Sci. USA, August 15, 2000, 97(17), 9591-9596						
	660	Lai J. S. et al., "Fluorinated DNA Bases as Probes of Electrostatic Effects in DNA Base Stacking," Angew. Chem. Int. Ed. (2003) 42: 5973-5977						
	661	Lai, J. S. et al., "Selective Pairing of Polyfluorinated DNA Bases," J. Am. Chem. Soc. (2004) 126(10): 3040-3041						
	662	Lane, A. N. et al., "NMR Assignments and Solution Conformation of the DNA-RNA Hybrid Duplex d(GTGAACTT)-r(AAGUUCAC)," Eur. J. Biochem., 1993, 215, 297-306						
	663	Larson, E.J., et al., "Rapid DNA fingerprinting of pathogens by flow cytometry," Cytometry, 2000, 41, 203-208						
	664	Larsson, M., et al., "High-throughput protein expression of cDNA products as a tool in functional genomics," J. Biotechnol., 2000, 80, 143-157						
	665	Le Doan et al., "Sequence-Targeted Chemical Modifications of Nucleic Acids by Complementary Oligonucleotides Covalently Linked to Porphyrins", Nucleic Acid Research, 1987, 15, 8643-8659						
	666	Lee et al., Cell, 1993, 75, 843-854						
	667	Lee, K. et al., "Ring-Constrained (N)-Methanocarba Nucleosides as Adenosine Receptor Agonists: Independent 5'-Uronamide and 2'-Deoxy Modifications," Bioorganic & Medicinal Chemistry Letters, 2001, 11(10), 1333-1337						
	668	Lee, Y. et al., "MicroRNA maturation: stepwise processing and subcellular localization," EMBO J. (2002) 21(17): 4663-4670						
	669	Lee, Y. et al., "The nuclearRNase III Drosha initiates microRNA processing," Nature (2003) 425: 415-419						
	670	Leeds, J.M. et al., "Pharmacokinetic Properties of Phosphorothioate Oligonucleotides," Nucleosides Nucleotides, 1997, 16(7-9), 1689-1693						
(	671	Letsinger et al., "Effects of Pendant Groups at Phosphorus on Binding Properties of D-ApA Analogues", Nucleic Acids Research, 1986, 14, 3487-3499						
	672	Letsinger, R.L. et al., "Cholesteryl-conjugated oligonucleotides: Synthesis, properties and activity as inhibitors of replication of human immunodeficiency virus in cell culture, Proc. Natl. Acad. Sci.,1989, 86, 6553-6556						
Examiner Signature		Date Considered						

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STA	LEMENT E	BY APPLIC	CANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	35	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS						
673	Lewis, D.L. et al., "Efficient delivery of siRNA for inhibition of gene expression in postnatal mice," Nature Genetics, 2002, 32, 107-108						
674	Li, S. et al., "Folate-Mediated Targeting of Antisense Oligodeoxynucleotides to Ovarian Cancer Cells," Pharm. Res. (1998) 15(10):1540-1545.						
675	Liao, "A pyrimidine-guanine sequence-specific ribonuclease from Rana catesbeiana (bullfrog) oocytes", Nucl. Acids Res., 1992, 20, 1371-1377						
676	Lima, W. F. et al., "Highly efficient endonucleolytic cleavage of RNA by a CyszHisz zinc-finger peptide," Proc. Natl. Acad. Sci. USA (1999) 96:10010-10015.						
677	Lima, W.F. et al., "Binding affinity and specificity of Escherichia coli RNase H1: impact on the kinetics of catalysis of antisense oligonucleotide-RNA hybrids," Biochemistry, Vol. 36, pages 390-398 (1997)						
678	Limbach, P.A. et al., "Summary: the modified nucleosides of RNA," Nucleic Acids Res., 1994, 22(12), 2183-2196						
679	Lin, KY. et al., "A Cytosine Analogue Capable of Clamp-Like Binding to a Guanine in Helical Nucleic Acids," J. Am. Chem. Soc., 1998, 120(33), 8531-8532						
680	Lin, KY. et al., "Tricyclic 2'-Deoxycytidine Analogs: Synthesis and Incorporation into Oligodeoxynucleotides Which Have Enhanced Binding to Complementary RNA," J. Am. Chem. Soc., 1995, 117, 3873-3874						
681	Lin, M. et al., "Inhibition of collagenase type I expression by psoralen antisense oligonucleotides in dermal fibroblasts," Faseb J. (1995), 9, 1371-1377						
682	Lipardi, C., et al., "RNAi as random degradative PCR: siRNA primers convert mRNA into dsRNAs that are degraded to generate new siRNAs," Cell, 2001, 107, 297-307						
683	Liu, H. et al."A Four Base Paired Genetic Helix with Expanded Size," Science (2003) 302; 868-871						
684	Liu, H. et al., "Toward a New Genetic System with Expanded Dimensions: Size-Expanded Analogues of Deoxyadenosine and Thymidine," J. Am Chem Soc. (2004) 126(4) 1102-1109						
685	Liu, K. et al., "Efficient Nuclear Delivery of Antisense Oligodeoxynucleotides and Selective Inhibition of CETP Expression by Apo E Peptide in a Human CETP-Stably Transfected CHO Cell Line," Arterioscler. Thromb. Vasc. Biol. (1999) 19:2207-2213.						
686	Lixin, R. et al., "Novel Properties of the Nucleolar Targeting Signal of Human Angiogenin," Biochem. Biophys. Res. Comm. (2001) 284:185-193.						
687	Loakes, D. et al., "The applications of universal DNA base analogues," Nucleic Acids Res., 2001, 29(12), 2437-2447						
688	Lukhtanov, E. A. et al., "Direct, Solid Phase Assembly of Dihydropyrroloindole Peptides with Conjugated Oligonucleotides," Bioconjugate Chem. (1996) 7(5):564-567.						

Examiner	Date	
Signature	Considered	

	1.4.40/DTO			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STA	LEMENT E	BY APPLIC	ANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	36	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS	
689	Madden, S.L., et al., "Serial analysis of gene expression: from gene discovery to target identification," Drug Discov. Today, September 2000, 5(9), 415-425	
690	Mahato et al., "Modulation of gene expression by antisense and antigene oligodeoxynucleotides and small interfering RNA," Expert Opinion on Drug Delivery, Jan. 2005, 2(1), 3-28	
691	Manche et al., "Interactions between double-stranded RNA regulators and the protein kinase DAI," Mol. Cell Biol., 1992, 12(11), 5238-5248	
692	Manoharan, M., "RNA interference and chemically modified small interfering RNAs," Current Opinion in Chemical Biology, 2004, 8, 570-579	
693	Manoharan M. et al., "Cholic Acid-Oligonucliotide Conjugates for Antisense Applications", Bioorganic Med. Chem. Letts., 1994, 4, 1053-1060	
694	Manoharan M. et al., "Oligonucleotide Conjugates: Alteration of the Pharmacokinetic Properties of Antisense Agents", Nucleosides and Nucleotides, 1995, 14, 969-973	
695	Manoharan, M. et al., "Chemical Modifications to Improve Uptake and Bioavailability of Antisense Oligonucleotides", Annals NY Acad. Sciences, 1992, 660, 306-309	
696	Manoharan, M. et al., "Introduction of a Lipophilic Thioether Tether in the Minor Groove of Nucleic Acids for Antisense Applications," Bioorg. Med. Chem. Letts., 1993, 3, 2765-2770	
697	Manoharan, M. et al., "Novel Functionalization of the Sugar Moiety of Nucleic Acids for Multiple Labeling in the Minor Groove," Tetrahedron Letters (1991) 32(49):7171-7174.	
698	Manoharan, M. et al., "Lipidic Nucleic Acids", Tetrahedron Letts., 1995, 36, 3651-3654	
699	Manoharan, M., "2'-Carbohydrate modifications in antisense oligonucleotide therapy: importance of conformation, configuration and conjugation," Biochimica et Biophysica Acta, 1999, 1489, 117-130	
700	Manoharan, M., "Designer Antisense Oligonucleotides: Conjugation Chemistry and Functionality Placement," Antisense Research and Applications, Crooke and Lebleu, eds., CRC Press Boca Raton. FL, 1993, Chapter 17, 303-349.	
701	Manoharan, M., "Oligonucleotide Conjugates as Potential Antisense Drugs with Improved Uptake, Biodistribution, Targeted Delivery and Mechanism of Action," Antisense Nucleic Acid Drug Development (2002) 12:103-128.	
702	Manoharan, M., "Oligonucleotide Conjugates in Antisense Technology," Antisense Drug Technology, Principles, Strategies, and Applications, Crooke, S. T. ed., Marcel Dekker, New York, (2001) Chapter 16, 391-467.	
703	Marcus-Sekura, "Comparative inhibition of chloramphenicol acetyltransferase gene expression by antisense oligonucleotide analogues having alkyl phosphotriester, methylphosphonate and phosphorothioate linkages", Nucleic Acids Res., 1987, 15, 5749-5763	

Examiner	Date	
Signature	Considered	

	1.1.10/DTO			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		I DISCLOS		Filing Date	02-20-2002	
STA <sup>-</sup>	TEMENT E	BY APPLIC	CANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	eets as necessary)		Examiner Name	Sean McGarry	
Sheet	37	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS
704	Marcus-Sekura, "Techniques for Using Antisense Oligodeoxyribonucleotides to Study Gene Expression", Anal. Biochemistry, 1988, 172, 289-295
705	Markiewicz, et al., "Simultaneous Protection of 3'- and 5'-Hydroxyl Groups of Nucleosides", Nucleic Acid Chemistry, Part 3, pgs. 229-231, L.B. Townsend, et al., Eds., J. Wiley and Sons, New York, 1986, 229-231
706	Martinez, J., et al., "Single-stranded antisense siRNAs guide target RNA cleavage in RNAi," Cell, 2002, 110, 563-574
707	Maruenda, H. et al., "Antisense Sequence-Directed Cross-Linking of DNA Oligonucleotides by Mitomycin C," Bioconjugate Chem. (1996) 7(5):541-544.
708	Maruenda, H. et al., "Antisense sequence-directed cross-linking of RNA oligonucleotides by mitomycin," Anti-Cancer Drug. Des. (1997) 12, 473-479
709	Marwick, C., "First "Antisense" Drug Will Treat CMV Retinitis," J. Am. Med. Assoc., 1998, 280(10), 871
710	Matsukura, M. et al., "Phosphorothioate Analogs of Oligodeoxynucleotides: Inhibitors of Replication and Cytopathic Effects of Human Immunodeficiency Virus", Proc. Natl. Acad. Sci. USA, 1987, 84, 7706-7710
711	Matteucci, M.D. et al., "Synthesis of Deoxyoligonucleotides on a Polymer Support," J. Am. Chem. Soc., 1981, 103(11), 3185-3191
712	McCafferey, A.P. et al., "RNA interference in adult mice," Nature, 2002, 418, 38-39
713	McIntyre, K.W. et al., "A Sense Phosphorothioate Oligonucleotide Directed to the Initiation Codon of Transcription Factor NF-kB p65 Causes Sequence-Specific Immune Stimulation," Antisense Res. Dev., 1993, 3, 309-322
714	McQueen, C.A. et al., "Effect of Nalidixic Acid on DNA Repair in Rat Hepatocytes," Cell Biol. Toxicol., 1989, 5(2), 201-206
715	Mellitzer et al., "Spatial and temporal 'knock down' of gene expression by electroporation of double-stranded RNA and morpholinos into early postimplantation mouse embryos," Mechanisms of Development, 2002, 118(1-2), 57-63
716	Meunier, L. et al., "The nuclear export signal-dependent localization of oligonucleopeptides enhances the inhibition of the protein expression from a gene transcribed in cytosol," Nucleic Acids Res. 1999, 27(13):2730-2736
717	Meyer, et al., "Efficient, Specific Cross-Linking and Cleavage of DNA by Stable, Synthetic Complementary Oligodeoxynucleotides", J. Am. Chem. Soc. 1989, 111, 8517-8519
718	Mili, S. et al., "Distinct RNP Complexes of Shuttling hnRNP Proteins with Pre-mRNA and rnRNA. Candidate Intermediates in Formation and Export of mRNA," Mol. Cell Biol. (2001) 21(21):7307-7319.

Examiner	Date	
Signature	Considered	

	1440/PT0			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STAT	LEMENT E	BY APPLIC	ANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	38	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS
719	Miller, et al., "A New Approach to Chemotherapy Based on Molecular Biology and Nucleic Acid Chemistry: Matagen (Masking Tape for Gene Expression", Anti-Cancer Drug Design, 1987, 2, 117-128
720	Miller, et al., "Biochemical and Biological Effects of Nonionic Nucleic Acid Methylphosphonates", Biochemistry 1981, 20, 1874-1880
721	Miller, et al., "Nonionic nucleic acid analogues. Synthesis and characterization of dideoxyribonucleoside methylphosphonates", Biochemistry 1979, 18, 5134-5143
722	Miller, et al., "Synthesis and properties of adenine and thymine nucleoside alkyl phosphotriesters, the neutral analogs of dinucleoside monophosphates", J. Am. Chem. Soc. 1971, 93, 6657-6664
723	Min, KL. et al., "Oligonucleotides comprised of alternating 2' -deoxy-2' -fluoro-beta-D-arabinonucleosides and D-2' -deoxyribonucleosides (2'F-ANA/DNA 'Altimers') induce efficient RNA cleavage mediated by RNase H," Bioorganic & Medicinal Chemistry Letters, September 2002, 12, 2651-2654
724	Mishra et al., "Improved leishmanicidal effect of phosphorotioate antisense oligonucleotides by LDL-medicated delivery", Biochim. Biophys. Acta, 1995, 1264, 229-237
725	Miura et al., "Fluorometric determination of total mRNA with oligo(dT) immobized on microtiter plates", Clin. Chem., 1996, 42(11), 1758-1764
726	Montgomery, M.K. et al., "RNA as a target of double-stranded RNA-mediated genetic interference in Caenorhabditis elegans," Proc. Natl. Acad. Sci. USA, 1998, 95(26), 15502-15507
727	Moran, S. et al., "A thymidine triphosphate shape analog lacking watson-crick pairing ability is replicated with high sequence selectivity," Proc. Natl. Acad. Sci. USA (1997) 94 10506-10511
728	Moran, S. et al., "Difluorotoluene, a Nonpolar Isostere for Thymine, Codes Specifically and Efficiently for Adenine in DNA Replication," J Am Chem Soc. (1997) 119(8), 2056-2057
729	Morita, K. et al., "2'-O,4'-C-Ethylene-Bridged Nucleic Acids (ENA): Highly Nuclease-Resistant and Thermodyamically Stable Oligonucleotides for Antisense Drug," Bioorganic & Medicinal Chemistry Letters, 2002, 12(1), 73-76
730	Morita, K. et al., "Synthesis and Properties of 2'-0,4'-C-Ethylene-Bridged Nucleic Acids (ENA) as Effective Antisense Oligonucleotides," Bioorg. Med. Chem., 2003, 11, 2211-2226
731	Moulds, C. et al., "Site and Mechanism of Antisense Inhibition by C-5 Propyne Oligonucleotides," Biochemistry, 1995, 34(15), 5044-5053
732	Napoli, C. et al., "Introduction of a Chimeric Chalcone Synthase Gene into Petunia Results in Reversible Co-Suppression of Homologous Genes in trans," Plant Cell, 1990, 2(4), 279-289
733	Nasevicius, A. et al., "Effective targeted gene 'knockdown' in zebrafish," Nature Genetics, 2000, 26, 216-220

Examiner	Date	
Signature	Considered	

		Complete if Known			
Substitute for 1449/PTO				Application Number	10/078,949
		DISCLOS		Filing Date	02-20-2002
STATEMENT BY APPLICANT			ANT	First Named Inventor	Stanley T. Crooke
				Art Unit	1635
(use as many sheets as necessary)				Examiner Name	Sean McGarry
Sheet	39	of	47	Attorney Docket Number	ISIS-5027

	NON PATENT LITERATURE DOCUMENTS	
734	Nelson, P. S. et al., "Bifunctional oligonucleotide probes synthesized using a novel CPG support are able to detect single base pair mutations," Nucleic Acids Res. (1989) 17(18):7187-7194	
735	Nestle, F.O. et al., "Cationic Lipid is not Required for Uptake and Selective Inhibitory Activity of ICAM-1 Phosphorothioate Antisense Oligonucleotides in Keratinocytes," J. Invest. Dermatol., 1994, 103, 569-575	
736	Nielsen et al., "Sequence-Selective Recognition of DNA by Strand Displacement with a Thymine-Substituted Polyamide," Science, 1991, 254, 1497-1500	
737	Nishikura, K. et al., "A Short Primer on RNAi: RNA-Directed RNA Polymerase Acts as a Key Catalyst," Cell, 2001, 107(4), 415-418	
738	Nykänen, A. et al, "ATP Requirements and Small Interfering RNA Structure in the RNA Interference Pathway," Cell, 2001, 107, 309-321	
739	Oberhauser et al., "Effective incorporation of 2'-O-methyl-oligonucleotides into liposomes and enhanced cell association through modification with thiocholesterol", Nucl. Acids Res., 1992, 20(3), 533-538	
740	Ogilvie, K.K. et al., "The Use of Silyl Groups in Protecting the Hydroxyl Functions of Ribonucleosides," Tetrahedron Letters, 1974, 15(33), 2861-2863	
741	Olie, R.A. et al., "Analysis of ribosyl-modified, mixed backbone analogs of a bcl-2/bcl-xL antisense oligonucleotide," Biochimica et Biophysica Acta, 1576 (2002), 101-109	
742	Olsen, D.B., et al., "Study of a Hammerhead Ribozyme Containing 2'-Modified Adenosine Residues," Biochemistry, 1991, 30:, 9735-9741	
743	O'Neill, B.M. et al., "A Highly Effective Nonpolar Isostere of Deoxyguanosine: Synthesis, Structure, Stacking, and Base Pairing," J. Org. Chem. (2002) 67(17):5869-5875	
744	Ørum, H. et al., "Locked nucleic acids: A promising molecular family for gene-function analysis and antisense drug development," Curr. Opin. Mol. Therap., 2001, 3(3), 239-243	
745	Outten, et al., "Synthetic 1-methoxybenzo[d]naphtho[1,2-b]pyran-6-one c-glycosides", J. Org. Chem. 1987, 52, 5064-5066	
746	Owen, et al., "Transcriptional activation of a conserved sequence element by ras requires a nuclear factor distinct from c-fos or c-jun", Proc. Natl. Acad. Sci USA, 1990, 87, 3866-3870	
747	Owen, G.R. et al., "4'-Substituted Nucleosides. 3. Synthesis of Some 4'-Fluorouridine Derivatives," J. Org. Chem., 1976, 41(18), 3010-3017	
748	Paddison, P.J., et al., "Stable suppression of gene expression by RNAi in mammalian cells," PNAS, 2002, 99(3), 1443-1448	
749	Parker, J.S. et al., "Structure insights into mRNA recognition from a PIWI domain-siRNA guide complex," Nature, 2005, 434, 663-666	

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
INFORMATION DISCLOSURE				Filing Date	02-20-2002	
STATEMENT BY APPLICANT			ANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet 40 of 47				Attorney Docket Number	ISIS-5027	

		NON PATENT LITERATURE DOCUMENTS
	750	Parkes, et al., "A short synthesis of 3'-cyano-3'-Deoxythymidine", Tetra. Lett., 1988, 29, 2995-2996
	751	Parr, W. et al., "Solid-Phase Peptide Synthesis on an Inorganic Matrix having Organic Groups on the Surface," Angew Chem. Internat. Edit, 1972, 11 (4), 314-315
	752	Patzel et al., "A Theoretical Approach to Select Effective Antisense Oligodeoxyribonucleotides at High Statistical Probability," Nucleic Acids Research (1999) pp. 4328-4334.
	753	Peracchi, A., "Prospects for antiviral ribozymes and deoxyribozymes," Rev. Med. Virol., Vol. 14, pages 47-64 (2004).
	754	Petersen, M. et al., "The conformations of locked nucleic acids (LNA)," J. Mol. Recognit., 2000, 13, 44-53
	755	Petersheim, et al., "Base-Stacking and Base-Pairing contributions to helix stability: thermodynamics of double-helix formation with CCGG, CCGGp, CCGGAp, ACCGGp, CCGGUp, and ACCGGUp", Biochemistry, 1983, 22, 256-263
	756	Pichon, C. et al., "Intracellular Routing and Inhibitory Activity of Oligonucleopeptides Containing a KDEL Motif," Mol. Pharmacol. (1997) 51:431-438.
	757	Pieken, W.A., et al., "Structure-Function Relationship of Hammerhead Ribozymes as Probed by 2'-Modifications," Nucleic Acids Symp Ser., 1991, 24, 51-53
	758	Pike et al., "Mixed Alkylation (Methylation and Ethylation) of Adenosine by Diazoethane in Aqueous 1,2-Dimethoxyethane," J. Org. Chem., 1974, 39(25), 3674-3676
	759	Pitts, A.E. et al., "Inhibition of human telomerase by 2'-O-methyl-RNA," Proc. Natl. Acad. Sci. USA, 1998, 95, 11549-11554
	760	Poopeiko, N.E. et al., "Xylo-configured Oligonucleotides (XNA, Xylo Nucleic Acid): Synthesis of Conformationally Restricted Derivatives and Hybridization Towards DNA and RNA Complements," Biorganic & Medicinal Chemistry Letters 2003, vol. 13, pages 2285-2290
	761	Prakash, T.P. et al., Abstract of The 227th ACS National Meeting, Anaheim,CA, March 28-April 1, 2004
	762	Prakash, T. P. et al., "Synthesis of Site-Specific Oligonucleotide-Polyamine Conjugates," Bioorg. Med. Chem. Lett. (1994) 4(14):1733-1738.
	763	Prashar, Y., et al., "A method for display of 3'-end fragments of restriction enzyme-digested cDnAs for analysis of differential gene expression," Methods Enzymol., 1999, 303, 258-272
	764	Puglisi, et al., "Absorbance melting curves of RNA", Methods in Enzymology, 1989, 180, 304-325
	765	Rajur, S. B. et al., "Covalent Protein-Oligonucleotide Conjugates for Efficient Delivery of Antisense Molecules," Bioconjugate Chem. (1997) 8(6):935-940.
	766	Rajwanshi, V.K., et al., "LNA stereoisomers: xylo-LNA (β-D-xylo configured locked nucleic acid) and α-L-ribo configured locked nucleic acid)," Chem. Commun., 1999, 1395-1396
Examiner Signature		Date Considered

0 L 111 L 5 L 1110/PT0		Complete if Known			
Substitute for 7	Substitute for 1449/PTO			Application Number	10/078,949
INFORMATION DISCLOSURE				Filing Date	02-20-2002
STATEMENT BY APPLICANT			CANT	First Named Inventor	Stanley T. Crooke
				Art Unit	1635
(use as many sheets as necessary)				Examiner Name	Sean McGarry
Sheet 41 of 47			47	Attorney Docket Number	ISIS-5027

	NON PATENT LITERATURE DOCUMENTS
767	Ranganathan, "Modification of the 21-Position of Purine Nucleosides: Synthesis of 21-a-Substituted-21-Deoxyadenosine Analogs", Tetrahedron Letters, 1977, 15, 1291-1294
768	Ransford et al., "2'-O-Ethyl Pyrimidine Nucleosides," J. Carbohydrates - Nucleosides - Nucleotides, 1974, 1(3), 275-278
769	Rao, et al., "A Novel One-step Procedure for the Conversion of Thymidine into 2,3'-Anhydrothymidine", J. Chem. Soc. Chem. Commun., 1989, 997-998
770	Rausch, J.W. et al., "Hydrolysis of RNA/DNA hybrids containing nonpolar pyrimidine isosteres defines regions essential for HIV type 1 polypurine tract selection," PNAS (2003) 100(20): 11279-11284
771	Reddy, M.P. et al., "Fast Cleavage and Deprotection of Oligonucleotides," Tetrahedron Letters, 1994, 35(25), 4311-4314
772	Reese, C.B. et al., "An Acetal Group Suitable for the Protection of 2'hydroxy Functions in Rapid Oligoribonucleotide Synthesis," Tetrahedron Letters, 1986, 27(20), 2291-2294
773	Renneberg, D. et al. "Antisense properties of tricyclo-DNA," Nucleic Acids Res., 2002, 30(13), 2751-2757
774	Renneberg, D., et al., "Watson—Crick base-pairing properties of tricycle-DNA," J. Am. Chem. Soc., 2002, 124, 5993-6002
775	Revankar et al., "Synthesis and Antiviral/Antitumor of Certain 3-Seazaguanine Nucleosides and Nucleotides", J. Med. Chem. 1984, 24, 1389-1396
776	Rhodes, J. et al., "Therapeutic potentiation of the immune system by costimulatory Schiffbaseforming drugs," Nature (1995) 377(6544):71-75.
777	Robins, et al., "Nucleic Acid Related Compounds. 42. A General Procedure for the Efficient Deoxygenation of Secondary Alcohols. Regiospecific and Stereoselective Conversion of Ribonucleosides to 2'-Deoxynucleosides", J. Am. Chem. Soc., 1983, 105, 4059-4065
778	Robins, et al., "Synthesis of 2'-Deoxytubercidin, 2'-Deoxyadenosine, and Related 2'-Deoxynucleosides via a Novel Direct Stereospecific Sodium Salt Glycosylation Procedure", J. Am. Chem. Soc., 1984, 106, 6379-6382
779	Roelen et al., "Synthesis of Nucleic Acid Methylphos-Phonothioates", Nucleic Acids Research 1988, 16(15), 7633-7645
780	Rottman et al., "Influence of 2'-O-Alkylation on the Structure of Single-Stranded Polynucleotides and the Stability of 2'-O-Alkylated Polynucleotide Complexes," Biochem., 1974, 13, 2762-2771
781	Ruby, et al., "An Early Hierarchic Role of U1 Small Nuclear Ribonucleoprotein in Splicesome Assembly", Science, 1988, 242, 1028-1035
782	Rump, E. T. et al., "Preparation of Conjugates of Oligodeoxynucleotides and Lipid Structures and Their interaction with Low-Density Lipoprotein," Bioconjugate Chem. (1998) 9(3):341-349.

Examiner	Date	
Signature	Considered	

0 L 111 L 5 L 1110/PT0		Complete if Known			
Substitute for 1449/PTO				Application Number	10/078,949
INFORMATION DISCLOSURE				Filing Date	02-20-2002
STATEMENT BY APPLICANT			CANT	First Named Inventor	Stanley T. Crooke
				Art Unit	1635
(use as many sheets as necessary)				Examiner Name	Sean McGarry
Sheet 42 of 47			47	Attorney Docket Number	ISIS-5027

	NON PATENT LITERATURE DOCUMENTS	
783	Ryan, et al., "Synthesis of 2-Thio-D-ribose and 2'-Thioadenosine Derivatives", J. Org. Chem., 1971, 36(18), 2646-2657	
784	Sambrook, et al., "Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory Press, 1989, Vol. 2, pgs. 11.31-11.32	
785	San et al., "Safety and short term toxicity of a novel cationic lipid formulation for human gene therapy", Human Gene Therapy, 1993, 4, 781-788	
786	Sanghvi, Y.S. et al., "Heterocyclic Base Modifications in Nucleic acids and their Applications in Antisense Oligonucleotides", Antisense Research and Applications, CRC Press, Boca Raton, Chapter 15, 1993, 273-288	
787	Scaringe, S.A. et al., "Novel RNA Synthesis Method Using 5'-O-Silyl-2'-O-orthoester Protecting Groups," J. Am. Chem. Soc., 1998, 120(45), 11820-11821	
788	Scaringe, S.A., "RNA Oligonucleotide Synthesis via 5'-Silyl-2'-Orthoester Chemistry," Methods, 2001, 23, 206-217	
789	Scaringe, S.A., Thesis entitled, "Design and Development of New Protecting Groups for RNA Synthesis," University of Colorado (1996)	
790	Scherer et al., "Approaches for the sequence-specific knockdown of mRNA," Nat. Biotechnol., 2003, 21(12), 1457-1465	
791	Schöning, KU., et al., "Chemical etiology of nucleic acid structure: the $\alpha$ -threofuranosyl-(3' $\rightarrow$ 2') oligonucleotide system," Science, 2000, 290, 1347-1351	
792	Schwartz, et al., "A microtransfection method using the luciferase-encoding reporter gene for the assay of human immunodeficiency virus LTR promoter activity", Gene, 1990, 88, 197-205	
793	Schwartz, M.E. et al., "Rapid Synthesis of Oligoribonucleotides Using 2'-O-(o-Nitrobenzyloxymethyl)-Protected Monomers," Bioorg. Med. Chem. Lett., 1992, 2(9), 1019-1024	
794	Schwarz, D.S. et al., "Asymmetry in the Assembly of the RNAi Enzyme Complex," Cell, 2003, 115(2), 199-208	
795	Schwarz, D.S., et al., "Evidence that siRNAs function as guides, not primers, in the Drosophila and human RNAi pathways," Molecular Cell, September 2002, 10(3), 537-548	
796	Searle, M. S. et al., "On the Stability of Nucleic Acid Structures in Solution: Enthalpy-Entropy Compensations, Internal Rotations and Reversibility," Nucl. Acids Res., 1993, 21(9), 2051-2056	
797	Seela, et al., "Palindromic Octa- and Dodecanucleotides Containing 2'-Deoxytubercidin: Synthesis, Hairpin Formation, and Recognition by the Endodeoxyribonuclease", Biochemistry, 1987, 26, 2232-2238	
798	Seliger, H., et al., "Synthetic Oligonucleotides for Biomedical Applications," Nucleic Acids Symp Ser., 1991, 24:193-196	

Examiner	Date	
Signature	Considered	

	1.4.40/DTO			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STA	STATEMENT BY APPLICANT			First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	43	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS	
799	Shea et al., "Synthesis, hybridization properties and antiviral activity of lipid- oligodeoxynucletide conjugates", Nucl. Acids Res., 1990, 18(13), 3777-3783	
800	Sheehan, D. et al., "Biochemical properties of phosphonoacetate and thiophosphonoactate oligodeoxyribonucleotides," Nucleic Acids Res., 2003, 31(14), 4109-4118	
801	Shi, Y., "Mammalian RNAi for the masses," Trends in Genetics (2003) 19(1): 9-12	
802	Sigman, "Nuclease Activity of 1,10-Phenanthroline-Copper Ion", Acc. Chem. Res., 1986, 19, 180-186	
803	Sijen, T. et al., "On the role of RNA amplification in dsRNA-triggered gene silencing," Cell, Nov. 16, 2001, 107, 465-476	
804	Singer et al., "Alkylation of Ribose in RNA Reacted with Ethylnitrosourea at Neutrality," Biochem., 1976, 15(23), 5052	
805	Singh, S.K. et al., "LNA (locked nucleic acids): synthesis and high-affinity nucleic acid recognition," Chem. Commun., 1998, 4, 455-456	
806	Singh, S.K., et al., "Synthesis of 2'-amino-LNA: a novel conformationally restricted high-affinity oligonucleotide analogue with a handle," J. Org. Chem., 1998, 63, 10035-10039	
807	Skorski, T. et al., "Antileukemia effect of c-myc N3'P5' phosphoramidate antisense oligonucleotides in vivo," Proc. Natl. Acad. Sci. USA, 1997, 94, 3966-3971	
808	Smith et al., "Antiviral effect of an oligo(nucleoside methylphosphonate) complementary to the splice junction of herpes simplex virus type 1 immediate early pre-mRNAs 4 and 5", Proc. Natl. Acad. Sci. USA, 1986, 83, 2787-2791	
809	Smith, T.F. et al., "Comparison of Biosequences," Adv. Appl. Math., 1981, 2, 482-489	
810	Song, E. et al., "RNA interference targeting Fas protects mice from fulmiant hepatitis," Nature Med., 2003, 9(3), 347-351	
811	Song, JJ. et al., "The Crystal Structure of Argonaute and Its Implication for RISC Slicer Activity," Science, 2004, 305, 1434-1437	
812	Song, JJ. et al., "The crystal structure of the Argonaute2 PAZ domain reveals an RNA binding motif in RNAi effector complexes," Nature Struct. Biol., 2003, 10(12), 1026-1032	
813	Soutschek, J. et al., "Therapeutic silencing of a endogenous gene by systemic administration of modified siRNAs," Nature, 2004, 432(7014), 173-178	
814	Sproat, et al., "Highly Efficient Chemical Synthesis of 2'-O-methylioligoribunocleotides and Tetrabiotinylated Derivatives; Novel Probes That are Resistant to Degradation by RNA or DNA Specific Nucleases", Nucleic Acids Research, 1989, 17, 3373-3386	

Examiner	Date	
Signature	Considered	

	1.1.10/DTO			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STA	STATEMENT BY APPLICANT			First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	44	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS
815	Sproat, et al., "New synthetic routes to protected purine 2'-O-methylriboside-3'-O-phosphoramidites using a novel alkylation procedure", Nucleic Acids Research, 1990, 18, 41-49
816	Steffens, R., et al., "168. Nucleic-acid analogs with constraint conformational flexibility in the sugar-phosphate backbone "tricycle-DNA'," Helv. Chim. Acta, 1997, 80, 2426-2439
817	Steffens, R., et al., "Synthesis and thermodynamic and biophysical properties of tricycle-DNA," Am. Chem. Soc., 1999, 121(14), 3249-3255
818	Stein, et al., "Oligodeoxynucleotides as Inhibitors of Gene Expression: A Review", Cancer Research, 1988, 48, 2659-2668
819	Stein, et al., "Physicochemical properties of phosphorothioate oligodeoxynucleotides", Nucleic Acids Research, 1988, 16, 3209-3221
820	Stufkens, et al., "Dynamic Jahn-Teller Effect in the Excited States of SeCl62-, SeBr62-, TeCl62- and TeBr62-", Recueil des Travaux Chimiques des Pays-Bas 1970, 89, 1185-1201
821	Suciu et al., "Synthesis of 9-(2,5-dideoxy-β-D-glycero-pent-4-enofuranosyl)adenine", Carbohydrate Research, 1975, 44, 112-115
822	Sui, G., et al., "A DNA vector-based RNAi technology to suppress gene expression in mammalian cells," PNAS, 2002, 99(8), 5515-5520
823	Sutcliffe, J.G. et al., "TOGA: An automated parsing technology for analyzing expression of nearly all genes," PNAS, 2000, 97(5), 1976-1981
824	Svinarchuk, F.P. et al., "Inhibition of HIV proliferation in MT-4 cells by antisense oligonucleotide conjugated to lipophilic groups," Biochimie, 1993, 75, 49-54
825	Tabara, H. et al., "RNAi in C. elegans: Soaking in the Genome Sequence," Science, 1998, 282(5388), 430-431
826	Table listing related applications and office actions and rejections from those related applications
827	Tamanini, F. et al., "The fragile X-related proteins FXRIP and FXRZP contain a functional nucleolar-targeting signal equivalent to the HIV-1 regulatory proteins," Hum. Mol. Genet. (2000) 9(10):1487-1493
828	Tang, XQ. et al., "2'-C-Branched Ribonucleosides: Synthesis of the Phosphoramidite Derivatives of 2'-C-Beta-Methylcytidine and Their Incorporation into Oligonucleotides," J. Org. Chem., 1999, 64(3), 747-754
829	Tazawa et al., "A Novel Procedure for the Synthesis of 2'-O-Alkyl Nucleotides" Biochem., 1972, 11(26), 4931
830	Thompson," Applications of Antisense and siRNAs During Preclinical Drug Development," DDT (2002) 7(17): 912-917

Examiner	Date	
Signature	Considered	

	4.40/DT0			Complete if Known		
Substitute for 1	449/PTO			Application Number	10/078,949	
	<del>_</del>	DISCLOS		Filing Date	02-20-2002	
STAT	TEMENT E	BY APPLIC	ANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	45	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS					
831	Tidd, D.M. et al., "Evaluation of N-ras oncogene anti-sense, sense and nonsense sequence methylphosphonate oligonucleotide analogues," Anti-Cancer Drug Design, 1988, 3(2), 117-127					
832	Tijsterman, M. et al., "RNA Helicase MUT-14-Dependent Gene Silencing Triggered in C. elegans by Short Antisense RNAs," Science, 295(5555), 694-697					
833	Timmons, L. et al., "Ingestion of bacterially expressed dsRNAs can produce specific and potent genetic interference in Caenorhabditis elegans," Gene, 2001, 263(1-2), 103-112					
834	Timmons, L. et al., "Specific interference by ingested dsRNA," Nature, 1998, 395(6705), 854					
835	To, KY. "Identification of differential gene expression by high throughput analysis," Comb. Chem. & High Throughput Screen, 2000, 3, 235-241					
836	Tuschl et al., "Targeted mRNA degradation by double-stranded RNA in vitro," Genes Dev, 1999, 13(24), 3191-3197					
837	U.S. Patent Application Serial No. 09/315,298 filed May 20, 1999, by Teng et al.					
838	U.S. Patent Application Serial No. 60/423,760 filed November 5, 2002, by Baker et al.					
839	Van der Krol, et al., "Modulation of Eukaryotic Gene Expression by Complementary RNA or DNA Sequences", BioTechniques, 1988, 6, 958-976					
840	Vickers, T.A. et al., "Efficient Reduction of Target RNAs by Small Interfering RNA and Rnase H-dependent Antisense Agents," J. Biol. Chem., 2003, 278(9), 7108-7118					
841	Wada, A. et al., "Nuclear export of actin: a novel mechanism regulating the subcellular localization of a major cytoskeletal protein," EMBO J. (1998) 17:1635-1641					
842	Wahlestedt, C., et al., "Potent and nontoxic antisense oligonucleotides containing locked nucleic acids," Proc. Natl. Acad. Sci. U.S.A., 2000, 97(10), 5633-5638					
843	Walder, et al., "Antisense DNA and RNA: Progress and Prospects", Genes & Development, 1988, 2, 502-504					
844	Walder, et al., "Role of RNase H in Hybrid-Arrested Translation by Antisense Oligonucleotides", Proc. Natl. Acad. Sci. USA 1988, 85, 5011-5015					
845	Wang, J., et al., "Cyclohexene nucleic acids (CeNA): Serum stable oligonucleotides that activate RNase H and increase duplex stability with complementary RNA," J. Am. Chem. Soc., 2000, 122, 8595-8602					
846	Wang, J., et al., "Syhthesis and binding property of an oligonucleotide containing tetrafluorophenoxazine," Tetrahedron Lett., 1998, 39, 8385-8388					
847	Wang, X. et al., "Modular Recognition of RNA by a Human Pumilio-Homology Domain," Cell (2002) 110:501-512.					

Examiner	Date	
Signature	Considered	

	1.4.40/DTO			Complete if Known		
Substitute for 1	1449/PTO			Application Number	10/078,949	
		DISCLOS		Filing Date	02-20-2002	
STA	STATEMENT BY APPLICANT			First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
	(use as many she	ets as necessary)		Examiner Name	Sean McGarry	
Sheet	46	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS
848	Wei, Z. et al., "Hybridization properties of oligodeoxynucleotide pairs bridged by polyarginine peptides," Nucleic Acids Res. (1996) 24(4):655-661.
849	Wein, G. et al., "The 3'-UTR of the mRNA coding for the major protein kinase C substrate MARCKS contains a novel CU-rich element interacting with MRNA stabilizing factors HuD and HuR," Eur. 1. Biochem. (2003) 270:350-365.
850	Wengel, J., et al., "LNA (locked nucleic acid)," Nucleosides, Nucleotides, 1999, 18(6 & 7), 1365-1370
851	Wianny et al., "Specific interference with gene function by double-stranded RNA in early mouse development," Nature Cell Biology (2000) 2: 70-75
852	Wilds, C.J., et al., "Duplex recognition by oligonucleotides containing 2'-deoxy-2'-fluoro-D-arabinose and 2'-deoxy-2'-fluoro-D-ribose. Intermolecular 2'-OH-phosphate contacts versus sugar puckering in the stabilization of triple-helical complexes," Bioconjugate Chem., 1999, 10, 299-305
853	Williams, D.M., et al., 'Properties of 2'-Fluorothymidine-Containing Oligonucleotides: Interaction with Restriction Endonuclease EcoRV," Biochemistry, 1991, 30, 4001-4009
854	Wolfe, S., et al., "The guache effect. Some stereochemical consequences of adjacent electron pairs and polar bonds," Acc. Of Chem. Res., 1972, 5, 102-111
855	Wouters, J. et al., "5-Substituted Pyrimidine 1,5-Anhydronhexitols: Conformational Analysis and Interaction with Viral Thymidine Kinase," Bioorg. Med. Chem. Lett., 1999, 9, 1563-1566
856	Wright, P. et al., "Large Scale Synthesis of Oligonucleotides via Phosphoramidite Nucleosides and a High-loaded Polystyrene Support," Tetrahedron Lett., 1993, 34(21), 3373-3376
857	Wu, H. et al., "Properties of Cloned and Expressed Human RNase H1," Journal of Biological Chemistry 1999, vol. 274, pages 28270-28278
858	Wu, X., et al., "Base-pairing systems related to TNA: α-threofuranosyl oligonucleotides containing phosphoramidate linkages," Organic Lett., 2002, 4(8), 1279-1282
859	Yang, Y. et al., "HIV-1 TAT-mediated protein transduction and subcellular localization using novel expression vectors," FEBS Letters (2002) 532, 36-44.
860	Yeung, et al., "Photoreactives and Thermal Properties of Psoralen Cross-Links", Biochemistry 1988, 27, 3204-3210
861	Yu, JY., et al., "RNA interference by expression of short-interfering RNAs and hairpin RNAs in mammalian cells," PNAS, 2002, 99(9), 6047-6052
862	Zamecnik, P.C. et al., "Inhibition of Rous sarcoma virus replication and cell transformation by a specific oligodeoxynucleotide," Proc. Natl. Acad. Sci. USA, 1978, 75(1), 280-284
863	Zamore, P.D. et al., "Ancient Pathways Programmed by Small RNAs," Science, 2002, 296, 1265-1269

Examiner	Date	
Signature	Considered	

Substitute for 1449/PTO				Complete if Known		
				Application Number	10/078,949	
INFORMATION DISCLOSURE				Filing Date	02-20-2002	
STATEMENT BY APPLICANT			CANT	First Named Inventor	Stanley T. Crooke	
				Art Unit	1635	
(use as many sheets as necessary)				Examiner Name	Sean McGarry	
Sheet	47	of	47	Attorney Docket Number	ISIS-5027	

	NON PATENT LITERATURE DOCUMENTS					
864	Zamore, P.D. et al., "RNAi: Double-Stranded RNA Directs the ATP-Dependent Cleavage of mRNA at 21 to 23 Nucleotide Intervals," Cell, 2000, 101, 25-33					
865	Zanta, M. A. et al., "Gene delivery: A single nuclear localization signal peptide is sufficient to carry DNA to the cell nucleus," Proc. Natl. Acad. Sci. USA (1999) 96:91-96.					
866	Zhang et al., "Single Processing Center Models for Human Dicer and Bacterial RNase III," Cell, 2004, 118, 57-68					
867	Zhang et al., "Targeted Gene Silencing by Small Interfering RNA-Based Knock-Down Technology," Current Pharmaceutical Biotechnology, 2004, 5, 1-7					
868	Zhang, H. et al., "Reduction of liver Fas expression by an antisense oligonucleotide protects mice from fuminant hepatitis," Nature Biotech., 2000, 18, 862-867					
869	Zhang, J., et al., "PowerBLAST: A new network BLAST application for interactive or automated sequence analysis and annotation," Genome Res., 1997, 7, 649-656					
870	Zhang, Z. et al., "Uptake of N-(4'-pyridoxyl)amines and release of amines by renal cells: A model for transporter-enhanced delivery of bioactive compounds," Proc. Natl. Acad. Sci. USA (1991) 88:10407-10410.					
871	Zhao et al., "Effect of different chemically modified oligodeoxynucleotides on immune stimulation," Biochemical Pharmacology, 1996, 51, 173-182					
872	Zhou, Y., et al., "Post-transcriptional suppression of gene expression in xenopus embryos by small interfering RNA," Nucleic Acids Res., 2002, 30(7), 1664-1669					
873	Zhu, T. et al., "Oligonucleotide-Poly-L-omithine Conjugates: Binding to Complementary DNA and RNA." Antisense Res. Dm. 119931 3:265-275.					
874	Zon, "Oligonucleotide Analogues as Potential Chemotherapy Agents", Pharm. Res., 1988, 5(9), 539-549					
875	Zon, "Synthesis of Backbone-Modified DNA Analogues for Biological Applications", J. Protein Chemistry, 1987, 6, 131-145					
876	Zuckermann, R. N. et al., "Site-Selective Cleavage of RNA by a Hybrid Enzyme," J. Am. Chem. SOC. (1988) 110:1614-1615.					

Examiner	Date	
Signature	Considered	